PQVPLRPMTYKAAVDLSHFL

QUERY	PQVPLRPMTYKAAVDLSHFL
CONSENSUS_A	----------g-f------
A.FR.HIV232956	---------F-G-L------
A.FR.HIV232957	---------F-G-F---F--
A.FR.HIV232959	---------F-G-F---F--
A.KE.Q23-CXC-CG	----------G--------
A.SE.SE6594	--------------------
A.SE.SE7253	-H---------G-L------
A.SE.SE7535	----------G-L------
A.SE.SE8131	----------G-L------
A.SE.SE8538	----------G-F------
A.SE.SE8891	----------G--------
A.UG.92UG037	----------F--GF--
A.UG.U455	----------F---F--
CONSENSUS_B	--------------------
B.-.E90NEF	----------G--------
B.-.HIV232997	----------L------
B.-.HIV233002	----------L------
B.-.HIV233009	----------G-L------
B.-.HIV233016	-K---------V---M----
B.-.HIV233020	--------------------
B.-.HIV233023	--I-----------------
B.-.HIV233029	----------G-L------
B.-.HIV233030	----------G--------
B.-.HIV233032	----------G--------
B.-.HIV233037	----------G-L------
B.-.HIV233038	--------------------
B.-.HIV233043	----------G--------
B.-.HIV233045	----------G-L------
B.-.HIV233046	----------G-L------
B.AU.1062-1-NEF	--------------------
B.AU.93JW-3	----------------P--
B.AU.93LW-3	--------------------
B.AU.AF064660	----------G-F--N---
B.AU.AF064667	---------FR---------
B.AU.AF064676	----------L-I----
B.AU.MBC200	--------------------
B.AU.MBC925	--------------------
B.CN.AF033570	----------G-L------
B.CN.AF033572	----------G-L--N---
B.CN.PRC8	---------F---L------
B.CN.RL42	----------G-L------
B.DE.D31	--------------------
B.DE.HAN	----------G-L------
B.DE.HEI28CS	---------x-G-x------
B.DE.HEI3BL	----------G-L------
B.DE.HEI4BL	--------------------
B.DE.HIVU52491	----------G-L------
B.DE.NEFCC	---------SR--R------
B.DE.NEFCG	---x-------G-L------
B.DE.NH53	--------------------
B.ES.89SP061	----------G-L------
B.ES.AF082355	--------------------
B.ES.AF082357	----------G-L------
B.ES.AF082358	----------G-L------
B.ES.AF082359	--------------F----
B.ES.AF082363	----------M-I----
B.ES.AF082364	--------------------
B.ES.AF082366	----------G-L------
B.ES.AF082368	----------G-L------
B.ES.AF082370	----------G--------
B.ES.AF082375	----------F---F--
B.ES.AF082376	----------G--------
B.ES.AF082377	--------------------
B.ES.AF082378	--------------------
B.ES.AF082380	--------------------
B.ES.AF082383	----------G-F------
B.ES.AF082386	--------------------
B.FR.HIV232961	--------------------
B.FR.HIV232962	----------G--------
B.FR.HIV232963	---------F-G-L------
B.FR.HIV232964	--------S----L------
B.FR.HIV232965	--------------------
B.FR.HXB2	--------------------
B.FR.NE100	---------RR--I------
B.FR.SWB884	---------RR--I------
B.GA.OYI	----------G-L------
B.GB.001GH-93(1)	----------G-M------
B.GB.002EM-93(1)	----------G-LN-----
B.GB.003PW-93(1)	-------I-----L------
B.GB.005PF1-93(1)	--------------------
B.GB.006DC-93(1)	----------G-F------
B.GB.010JW-93(1)	----------G-L------
B.GB.011JR-93(4)	----------G-L------
B.GB.012WM-93(1)	------------F------
B.GB.013PP-94(2)	--I-------Q--L------
B.GB.016GB-93(1)	----V-----R--R-F----
B.GB.023PA-93(1)	L------------F------
B.GB.025JN-93(1)	----------G-F---Y--
B.GB.027SL-93(1)	--------------------
B.GB.028JH-94(1)	----------G-L------
B.GB.030JG-93(1)	----------L------
B.GB.031DA-93(1)	----V------G-L------
B.GB.032AN-93(1)	----------R--L------
B.GB.037BS-94(2)	----------R---------
B.GB.039NM-94(1)	--I--------G-L------
B.GB.044C1-94(2)	----------G--------
B.GB.046JM-94(1)	----------L------
B.GB.048AD-94(1)	----------G-L------
B.GB.056RP-94B(1)	--------I--G-F------
B.GB.057DR-94(1)	----------G--------
B.GB.065RK-94(1)	--------------------
B.GB.067MM-94(2)	----------G-F---Y--
B.GB.068JB-94(1)	L-------------------
B.GB.098MS-94(1)	--------------------
B.GB.103CD-94(1)	----------G-L------
B.GB.104RT-94(1)	----------G--------
B.GB.105AS-94(1)	----------G-L--T---
B.GB.112CR-94(2)	--------I--G-L------
B.GB.117CH-94(2)	--------------------
B.GB.122PS-95(1)	----------G-L------
B.GB.124PD-95(1)	--------------------
B.GB.127RG-96(1)	--------D--G--------
B.GB.130WDC-95(1)	--------------L------
B.GB.131MVS-95(1)	---------------I----
B.GB.143PL-95(1)	-H----------L------
B.GB.151DH-95(1)	--------------------
B.GB.157GT-95(1)	--------N--G--------
B.GB.160KO-95(1)	--------------------
B.GB.161KC-95(1)	----------G-L------
B.GB.162BB-95(1)	--------------------
B.GB.163NG-95(1)	-------I--R--L------
B.GB.164SZ-95(1)	----------G-I------
B.GB.165DH-95(1)	----------G-L------
B.GB.166PW-95(1)	----------G-L------
B.GB.167RW-95(1)	---------F-G-L------
B.GB.168MB-95(1)	----------G--------
B.GB.CAM1	-------------L-I----
B.GB.GLNEF1	--------------------
B.GB.MANC	---------F-G-L------
B.GB.NEF2	----V---------------
B.GB.NEF3	--------------------
B.GB.NEF5	--------------------
B.IN.HIVP35A	----------G-L------
B.IT.AF011471	--E-----------------
B.IT.AF011474	----------G-F------
B.IT.AF011477	----------RG-L------
B.IT.AF011478	----------RGxL------
B.IT.AF011480	-----x--------------
B.IT.AF011482	T------------L------
B.IT.AF011483	----------G-L------
B.IT.AF011486	----------Q--L------
B.IT.AF011488	x---------R--R------
B.IT.AF011492	----------G-L------
B.IT.AF047080	----------S--------
B.IT.AF047081	----------G--------
B.IT.B.IT-L1	--------x----L------
B.IT.B.IT-L2	--------------------
B.IT.B.IT-L3	---------HR--I------
B.IT.B.IT-L4	---------------M----
B.IT.B.IT-L5	---x-------S-----x--
B.IT.B.IT-R1	-------------L------
B.IT.B.IT-R2	----------G-L------
B.IT.B.IT-R3	----------Q--xN-----
B.IT.B.IT-R4	----------G--------
B.IT.B.IT-R5	-------x-CR--I------
B.KR.AF063915	----------G-L------
B.KR.AF063916	--------------------
B.KR.AF063919	----------G-F------
B.KR.AF063921	-------------------I
B.KR.AF063926	----------G-L------
B.KR.AF063927	--------------------
B.KR.AF063931	-------------L------
B.KR.HIVZ98019	--------------------
B.KR.HIVZ98022	----------G--------
B.KR.HIVZ98024	----------G-L------
B.KR.HIVZ98025	--------------------
B.KR.HIVZ98027	----------G-L------
B.KR.HIVZ98029	----------G-L------
B.KR.HIVZ98030	------------S-------

```
B.KR.HIVZ98032        -----------G-S------
B.KR.HIVZ98034        --------D--SS-------
B.NL.3202A21          -----------G-L------
B.NL.NEFA             ------------L------
B.NL.NEFD             -----------G-L------
B.NL.NEFE             ------------F------
B.SE.AF047082         ------------L------
B.SE.AF047083         -----------G--------
B.SE.AF047085         ------------F------
B.TH.28-19            -----------G-L------
B.TH.AF082838         -----------G-L------
B.TH.AF082839         --------------------
B.TH.AF082841         ------------F------
B.TW.LM49             --------D--G-I------
B.US.HIV1U03375       -----------G-L------
B.US.005PF-96(1)      --------------------
B.US.AD-93(1)         -----------G-L------
B.US.AD8              --------------------
B.US.BC               -------I-------I----
B.US.BIB              -----------G-R---W--
B.US.BJ-93(1)         --------------------
B.US.BO1              --------------------
B.US.BRVA             --------------------
B.US.BT-94(1)         -R------------------
B.US.CD1              --------------------
B.US.D8511            -----------G-L------
B.US.DH1              -----------G-L------
B.US.DH123            --I----------L------
B.US.DJ-93(1)         --------------------
B.US.E1               -----------G-L------
B.US.E81NEF           -----------G--------
B.US.E88NEF           -----------G--------
B.US.EP-94(1)         ---------W---L------
B.US.FA-93(1)         -----------G--------
B.US.HIV1U16893       ------------L------
B.US.HIV1U24455       -----------G--------
B.US.HIV1U26074       --------------------
B.US.HIV1U26098       --------------------
B.US.HIV1U26112       -----------G-L------
B.US.HIV1U26119       --------------------
B.US.HIV1U26141       --------------------
B.US.HIVU44444        ---------------I----
B.US.HIVU44450        -----------G-L------
B.US.HIVU44456        -----------G--------
B.US.HIVU44465        -----------G-L------
B.US.HIVU44468        --------------------
B.US.HP87B1           -----------G-L------
B.US.HS-93(1)         ------------L------
B.US.JRCSF            ------------I------
B.US.JRFL             -----------G--------
B.US.LM1              -----------G-L------
B.US.LT-87-1(1)       -----------G-L------
B.US.MB-94(1)         -------V---G--------
B.US.MNCG             ------------L------
B.US.NC7              ------------GI------
B.US.NEF              --------------------
B.US.NEF164B          ------------I-M-----
B.US.NEF166E          -----------G-L------

B.US.NEF179C          -----------G-L------
B.US.NEF226B          -------V------------
B.US.P102A13          --------------------
B.US.P233A17          -----------G-L------
B.US.P248A01          --------------------
B.US.P357A01          -----------G-L------
B.US.P896             --------------------
B.US.PC-93(1)         -----------G--------
B.US.PRISO(1)         -H------------------
B.US.RF               ---------F----------
B.US.RP12             --------------------
B.US.RR1              --------------------
B.US.SC               --------------------
B.US.SF2              -------------L-I----
B.US.U16917           --------S------I----
B.US.WEAU160          -------------H-----#
B.US.WR27             --------------------
B.US.YU2              ---------H---M------

CONSENSUS_C           -----------g-f---f--
C.BR.92BR025          ------------V----F--
C.BW.96BW01B21        -----------G-F--GF--
C.BW.96BW0402         ----------------F---
C.BW.96BW0502         -----------G-F--GF--
C.BW.96BW1104         -------------FG--F--
C.BW.96BW1210         -----------G-F---F--
C.BW.96BW15B03        -----------G-----F--
C.BW.96BW16B01        -----------E-F---F--
C.BW.96BW17A09        -------------F---F--
C.ET.ETH2220          -------------F---L--
C.FR.HIV232966        ---------F-G-F---F--
C.FR.HIV232967        ---------F-G-F--GF--
C.FR.HIV232968        --------S----F---F--
C.FR.HIV232969        --------S--S-F---F--
C.FR.HIV232970        --------S----F---F--
C.FR.HIV232971        -------------F--GF--
C.FR.HIV232972        -------------F-FGF--
C.FR.HIV232973        ----------------W--
C.FR.HIV232976        -------------F---F--
C.FR.HIV232977        ----------------W--
C.FR.HIV232978        -------------F---F--
C.FR.HIV232979        -----------G-F---F--
C.FR.HIV232980        ----------------F--
C.FR.HIV232996        -----------G-F---F--
C.IN.21068            ---------F-G-L---F--
C.IN.301904           ---------F-E-----F--
C.IN.301999           ---------F-G-F---F--
C.IN.94IN11246        ---------F-G-F---F--
C.IN.HIVY15117        -----------G-F---F--
C.IN.HIVY17884        ---------F-G-F---F--
C.IN.HIVY17891        ---------F-G-F---F--
C.IN.HIVY17892        ---------F-G-F---F--

CONSENSUS_D           -----------e--------
D.CD.84ZR085          --------------------
D.CD.ELI              -----------E-L------
D.CD.NDK              -----------E--------
D.UG.94UG1141         -----------E--------

CONSENSUS_F           --------------------
F.CM.HIV232985        --------------------
F.CM.HIV232986        -------------L------
F.FR.HIV232987        ---------F----------

CONSENSUS_F1          -----------?--------
F1.BE.VI850           ----V---------------
F1.BR.93BR020.1       -----------G--------
F1.FI.FIN9363         -----------G-F---Q-x
F1.FR.MP411           ---------F----------

CONSENSUS_F2          -------------?------
F2.CM.MP255           --------------------
F2.CM.MP257           -------------L------

CONSENSUS_G           -------------f---F--
G.BE.DRCBL            -------------F---F--
G.FI.HH8793           ----V--------F---F--
G.ML.HIV232990        -------------L---F--
G.NG.92NG083          -------------F---F--
G.NG.HIV232991        --L--------G-F---F--
G.NG.HIV232992        -----------G-F---F--
G.SE.SE6165           ---------F-G-F---F--

CONSENSUS_H           -----------g-f------
H.BE.VI991            -----------G-F------
H.BE.VI997            -------------L------
H.CD.HIV232994        -----------E-F-F-F--
H.CD.HIV232995        ----V------G-L-F----
H.CF.90CF056          -----------G-F------

CONSENSUS_J           --?--------G-?---F--
J.SE.SE9173           --x--------G-F---F--
J.SE.SE9280           --I--------G-----F--

CONSENSUS_K           ---------?-?-F--GF--
K.CD.EQTB11C          ---------F-G-F--GF--
K.CM.MP535            -------------F--GF--
N.CM.YBF30            -------I---Q-F---F--

CONSENSUS_O           ---------?-?-F---F--
O.CM.ANT70C           -----------G-F---F--
O.CM.MVP5180          ---------F---F---F--
CRF01_AE.CF.90CF402   -----------G-F---F--
CRF01_AE.FR.232982    -----------G-F---F--
CRF01_AE.FR.232983    -----------G-F---F--
CRF01_AE.FR.232984    ---------F-E-F---F--
CRF01_AE.TH.1-2       ---------F-E-F---F--
CRF01_AE.TH.1-3       ---------F-E-F---F--
CRF01_AE.TH.11-25     -H-------F-G-F---F--
CRF01_AE.TH.11-31     ---------F-G-F---F--
CRF01_AE.TH.122-21    -----------G-F---F--
CRF01_AE.TH.18-47     -------------F---F--
CRF01_AE.TH.235-3     -----------G-F---F--
CRF01_AE.TH.235-32    -----------G-F---F--
CRF01_AE.TH.24-54     -----------G-F---F-F
CRF01_AE.TH.240-12    -----------G-F-F-F--
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CRF01_AE.TH.26-3      -----------G-F---F--
CRF01_AE.TH.35-6      -----------G-F---F--
CRF01_AE.TH.6-9       -----------G-F---F--
CRF01_AE.TH.73-44     ---------F-G-F---F--
CRF01_AE.TH.74-26     -------------F---F--
CRF01_AE.TH.89-30     ---------F-G-F---F--
CRF01_AE.TH.9-3       -----------G-F---F--
CRF01_AE.TH.93TH253   -----------G-F---F--
CRF01_AE.TH.98-4      -----------G-F---F--
CRF01_AE.TH.CM240     -----------G-F---F--
CRF01_AE.TH.TH022     -----------G-F---F--
CRF01_AE.TH.TH047     ---------F-E-F---F--
CRF02_AG.FR.DJ263     -------------F--GF--
CRF02_AG.FR.DJ264     -----------G-F--GF--
CRF02_AG.NG.IBNG      -----------G--------
CRF03_AB.RU.KAL1532   -----------G-F------
CRF04_cpx.CY.94CY03   ---------F-G-L------
CRF04_cpx.GR.97PVCH   ---------F---L------
CRF04_cpx.GR.97PVMY   --------------------
AC.IN.21301           -----------G-L---F--
AC.RW.92RW009         -----------------F--
AC.SE.SE9488          -----------G-L------
AC.ZM.ZAM184          -----------G--------
ACD.SE.SE8603         -----------------F--
AD.SE.SE6954          -----------G--------
AD.SE.SE7108          --------------------
ADHU.NO.NOGIL3        --------------------
ADU.CD.MAL            -----------G-F------
AF.GA.HIV232981       -----------G-F------
AG.NG.G3              Q-----------F---F--
AG.SE.SE7812          --------------------
AGHU.GA.VI354         --L------F-G-F--GF--
AGJ.AU.BFP90          ----V--------F---F--
AGJ.ML.95ML84         ---------F-G-F---F--
AGU.CD.Z321           ---------F-G-F---F--
BF.BR.93BR029.4       -----------G-L------
DF.BE.VI961           ---------F-G-L------
GH.GA.HIV232993       -----------G-F--GF--
GU.FR.HIV232974       -----------G-F------
U.CD.VI1126           -----------G-F-----I
U.CM.HIV232988        -------------F--GF--
U.FR.HIV232958        -----------G-F--GF--
U.FR.HIV232960        -----------G-F--GF--

CONSENSUS_CPZ         ----?------?-F--??--
CPZ.GA.CPZGAB         ----T--------F------
CPZ.US.CPZUS          -----------Q-F--GF--
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MFSALSEGATPQDLNTMLNT

QUERY	MFSALSEGATPQDLNTMLNT
CONSENSUS_A	----------m---i
A.KE.Q23-CXC-CG	----------M---I
A.SE.SE6594	----------M---I
A.SE.SE7253	V----------M---I
A.SE.SE7535	----------M---I
A.SE.SE8131	----------H---M---I
A.SE.SE8538	----------I
A.SE.SE8891	----------G---M---I
A.UG.92UG037	----------M---I
A.UG.U455	----------M---V
CONSENSUS_B	----------
B.AU.AF128998	----------
B.-.NL43E9	----------
B.AU.MBC18	----------
B.AU.MBC200	----------
B.AU.MBC925	----------
B.AU.MBCC54	----------
B.AU.MBCC98	----------
B.AU.MBCD36	--T----------
B.CN.RL42	----------
B.DE.D31	----------
B.DE.HAN	----------
B.ES.89SP061	----------
B.FR.HXB2	----------
B.GA.OYI	-----A----------
B.GB.CAM1	----------
B.GB.MANC	---------I----------
B.JP.JH31	----------
B.NL.3202A21	----------
B.TW.LM49	----------
B.US.85WCIPR54	----------
B.US.AD8	----------
B.US.BC	----------
B.US.DH123	----------
B.US.JRCSF	----------
B.US.JRFL	----------
B.US.MNCG	----------
B.US.NC7	----------
B.US.NY5CG	----------
B.US.P896	----------
B.US.RF	----------
B.US.SF2	----------
B.US.WC001	----------
B.US.WEAU160	----------
B.US.WR27	----------Y-----
B.US.YU2	----------
CONSENSUS_C	--T----------
C.BR.92BR025	--T----------
C.BW.96BW01B22	--T----------
C.BW.96BW0402	--T----------
C.BW.96BW0502	--T----------
C.BW.96BW1104	--T----------T-
C.BW.96BW1210	--T----------
C.BW.96BW15B03	--T----------
C.BW.96BW1626	--T----------
C.BW.96BW17A09	--T----------
C.ET.ETH2220	--T----------
C.IN.93IN904	--T----------
C.IN.93IN905	--T----------
C.IN.93IN999	--T----------
C.IN.94IN11246	--T----------
C.IN.95IN21068	--T----------
CONSENSUS_D	----------
D.CD.84ZR085	----------
D.CD.ELI	----------
D.CD.NDK	----------
D.CD.Z2Z6	----------
D.UG.94UG1141	----------
CONSENSUS_F	----------
F.BR.BZ162	----------
F.CD.VI174	----------
F.RW.VI69	----------
CONSENSUS_F1	----------
F1.BE.VI850	----------T---------
F1.BR.93BR020.1	----------
F1.FI.FIN9363	----------
F1.FR.MP411	----------
CONSENSUS_F2	----------
F2.CM.MP255	----------
F2.CM.MP257	----------
CONSENSUS_G	----------xx-
G.BE.DRCBL	--T----------
G.FI.HH8793	----------
G.NG.92NG083	----------
G.SE.SE6165	----------L----
CONSENSUS_H	----------A----
H.BE.VI991	----------A----
H.BE.VI997	----------A----
H.CF.90CF056	----------A----
CONSENSUS_J	----------
J.SE.SE9173	----------
J.SE.SE9280	----------
CONSENSUS_K	----------
K.BE.VI325	-----AD----------
K.CD.EQTB11C	----------
K.CM.MP535	--T----------
N.CM.YBF30	--M--------S--------
CONSENSUS_O	--M------??Y-I-----A
O.CM.ANT70C	--M------ISY-I-----A
O.CM.MVP5180	--M------V-Y-I-----A
CRF01-AE.CF.90CF40	----------M---I
CRF01-AE.TH.93TH25	----------M---I
CRF01-AE.TH.CM240	----------M---I
CRF01-AE.TH.TH022	----------M---I
CRF01-AE.TH.TH047	----------M---I
CRF02_AG.FR.DJ263	--T----------M---I
CRF02_AG.FR.DJ264	--T----------M---I
CRF02_AG.NG.IBNG	----------M---I
CRF03_AB.RU.KAL15	----------M---I
CRF04_cpx.CY.94CY0	----------M---I
CRF04_cpx.GR.97PVC	----------M---I
CRF04_cpx.GR.97PVM	----------M---I
AC.ET.E3099G	----------
AC.IN.21301	--T----------
AC.RW.92RW009	--T----------
AC.SE.SE9488	--T----------
AC.ZM.ZAM174-21	--T----------
AC.ZM.ZAM184	----------
AC.ZM.ZAM716-17	--T----------
ACD.SE.SE8603	----------M---I
AD.SE.SE6954	---------A--------S-
AD.SE.SE7108	----------M---I
ADHU.NO.NOGIL3	------D--------M---I
ADU.CD.MAL	----------M---I
AG.NG.G3	--T----------
AG.SE.SE7812	----------M---I
AGHU.GA.VI354	----------M---I
AGJ.AU.BFP90	--T----------M---I
AGJ.ML.95ML8	----------M---I
AGU.CD.Z321	----------
BF.BR.93BR029.4	----------
DF.CD.VI961	--T----------
U.CD.VI1126	--T----------
CONSENSUS_CPZ	----------v-----A
CPZ.CD.CPZANT	----------H-------A
CPZ.GA.CPZGAB	---------L---V-----A
CPZ.US.CPZUS	--M----------V-----A

WYQLEKEPIVGAETFYVDGA

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QUERY                WYQLEKEPIVGAETFYVDGA

CONSENSUS_A          ------D--a----------
A.KE.Q23-CXC-CG      ------D--A----------
A.SE.SE6594          --L--ED-----DS-F-E--
A.SE.SE7253          ------D--A----------
A.SE.SE7535          ------D-------------
A.SE.SE8131          ------D--A-V--------
A.SE.SE8538          ------D--A----------
A.SE.SE8891          ------D-------------
A.UG.92UG037         ------D--A----------
A.UG.U455            ------D--A----------

CONSENSUS_B          --------------------
B.-.NL43E9           ---------I----------
B.AU.MBC18           ---------T----------
B.AU.MBC200          --------------------
B.AU.MBC925          ---------I----------
B.AU.MBCC54          ---------I----------
B.AU.MBCC98          -----R---I----------
B.AU.MBCD36          ---------I-------N--
B.CN.RL42            ---------EE---------
B.DE.D31             -----T--------------
B.DE.HAN             --------------------
B.FR.HXB2            --------------------
B.GA.OYI             ------D-------------
B.GB.CAM1            --------------------
B.GB.MANC            --------------------
B.NL.3202A21         --------------------
B.TW.LM49            ---------I----------
B.US.AD8             --------------------
B.US.BC              ---------E----------
B.US.DH123           --------------------
B.US.JRCSF           --------------------
B.US.JRFL            --------------------
B.US.MNCG            --------------------
B.US.NY5CG           ---------I----------
B.US.P896            --------------------
B.US.RF              ---------I----------
B.US.SF2             --------------------
B.US.WEAU160         --------------------
B.US.WR27            --------------------
B.US.YU2             ---------I----------

CONSENSUS_C          ---------a----------
C.BR.92BR025         ---------A----------
C.BW.96BW01B03       --------------------
C.BW.96BW0402        ---------A----------
C.BW.96BW0502        ---------P-V--------
C.BW.96BW1104        -----T--MA----------
C.BW.96BW1210        ---------A-V--------
C.BW.96BW15B03       ---------I----------
C.BW.96BW1626        --------------------
C.BW.96BW17A09       ------D--A----------
C.ET.ETH2220         ---------A-V--------
C.IN.21068           ---------A----------
C.IN.301904          ------D--A-V--------
C.IN.301905          ------D--A-V--------
C.IN.301999          --R------A-V--------
C.IN.94IN11246       ------D--A----------

CONSENSUS_D          ---------i----------
D.CD.84ZR085         ---------I----------
D.CD.ELI             ---------I----------
D.CD.NDK             ---------I----------
D.CD.Z2Z6            ---------I----------
D.UG.94UG1141        --------------------

CONSENSUS_F1         -----T---a----------
F1.BE.VI850          -----T---A--D-------
F1.BR.93BR020.1      -----T--------------
F1.FI.FIN9363        -----T---A----------
F1.FR.MP411          -----T---I----------

CONSENSUS_F2         -----T---?----------
F2.CM.MP255          -----T---A----------
F2.CM.MP257          -----T---I----------

CONSENSUS_G          --?--T---P----Y-----
G.BE.DRCBL           -----T---P-V--Y-----
G.FI.HH8793          --R--T---P----Y-----
G.NG.92NG083         -----T---P----Y-----
G.SE.SE6165          --R--T---P----Y-----

CONSENSUS_H          -----t---a----Y-----
H.BE.VI991           -----T---E----Y-----
H.BE.VI997           -----A---A----Y-----
H.CF.90CF056         -----T---A----Y-I---

CONSENSUS_J          ---------M----------
J.SE.SE9173          ---------M----------
J.SE.SE9280          ---------M----------

CONSENSUS_K          -----T--------------
K.CD.EQTB11C         -----T--------------
K.CM.MP535           -----T--------------
N.CM.YBF30           -----T---S----------

CONSENSUS_O          --?--?---?----?-----
O.CM.ANT70C          --R--S---M----Y-----
O.CM.MVP5180         -----T--------------
AC.ET.E3099G         ------D----------xDT
AC.IN.21301          --------MA----------
AC.RW.92RW009        ---------L----------
AC.SE.SE9488         ------D--I----------
AC.ZM.ZAM184         ---------AR---------
ACD.SE.SE8603        ------D--I----------
AD.SE.SE6954         ------D-M----------
AD.SE.SE7108         ------D--A-V--------
ADU.CD.MAL           -----T--------------
AG.NG.G3             --R--T---P----Y-----
AG.SE.SE7812         ------D-------------
AGHU.GA.VI354        -----T--------------
AGHU.NO.NOGIL3       -----T--------------
AGJ.AU.BFP90         -----T--------------
AGJ.ML.95ML8         -----T--------------
AGU.CD.Z321          ---------I----------
BF.BR.93BR029.4      --------------------
CRF01_AE.CF.90CF40   ------D--M----------
CRF01_AE.TH.93TH25   ------D-------------
CRF01_AE.TH.CM240    ------D-------------
CRF01_AE.TH.TH022    ------D-------------
CRF01_AE.TH.TH047    ---------I----------
CRF02_AG.FR.DJ263    ------D-------------
CRF02_AG.FR.DJ264    ------D-------------
CRF02_AG.NG.IBNG     ------D-------------
CRF03_AB.RU.KAL153   --------------------
CRF04_CPX.CY.94CY0   -----TD--A----------
CRF04_CPX.GR.97PVC   $----PD--A----------
CRF04_CPX.GR.97PVM   -----T---A----------
DF.CD.VI961          ---------M----------
U.CD.VI1126          -----TD--A----------

CONSENSUS_CPZ        --?--t---p?---------
CPZ.CD.CPZANT        --N-LAD--PE---------
CPZ.GA.CPZGAB        --S--T---PTTD-Y-----
CPZ.US.CPZUS         --K--T-A-E----------
```

Study Subject ID:00RCH86
Study Subject Clone:
Study Subject HLA:A34,A74,B53,B81,Cw4,Cw8
Sequence: Known reactive 20Mer0: PQVPLRPMTYKAAVDLSHFL Nef(72–91)

Possible HLA

A34	A*3401,A*3402
A74	A*7401,A*7402
B53	B*5301
B81	B*8101
Cw4	C4,Cw*0401,C*0401,Cw*0402
Cw8	Cw*08,Cw*0801,Cw*0802,C*0802,Cw*0803

Possible Epitopes based on anchor residues

(6-14)	RPMTYKAAV	B*5301
(3-10)	VPLRPMTY	B*5301
(9-16)	TYKAAVDL	Cw*0401

Anchor Residues Searched

B*5301	X[P]XXXXXX[LIVMY]
B*5301	X[P]XXXXX[LIVMY]
B*5301	X[P]XXXXXXX[LIVMY]
Cw*0401	X[YPF]XXXXXX[LF]
Cw*0401	X[YPF]XXXXX[LF]
Cw*0401	X[YPF]XXXXXXX[LF]

Study Subject ID:00RCH86
Study Subject Clone:
Study Subject HLA:A34,A74,B53,B81,Cw4,Cw8
Sequence: Known reactive 20Mer1: MFSALSEGATPQDLNTMLNT p24(39–58)

Possible HLA

A34	A*3401,A*3402
A74	A*7401,A*7402
B53	B*5301
B81	B*8101
Cw4	C4,Cw*0401,C*0401,Cw*0402
Cw8	Cw*08,Cw*0801,Cw*0802,C*0802,Cw*0803

Possible Epitopes based on anchor residues

(9-17)	TPQDLNTML	B*5301
(9-16)	TPQDLNTM	B*5301
(9-17)	TPQDLNTML	Cw*0401

Anchor Residues Searched

B*5301	X[P]XXXXXX[LIVMY]
B*5301	X[P]XXXXX[LIVMY]
B*5301	X[P]XXXXXXX[LIVMY]
Cw*0401	X[YPF]XXXXXX[LF]
Cw*0401	X[YPF]XXXXX[LF]
Cw*0401	X[YPF]XXXXXXX[LF]

Study Subject ID:00RCH86
Study Subject Clone:
Study Subject HLA:A34,A74,B53,B81,Cw4,Cw8
Sequence: Known reactive 20Mer2: WYQLEKEPIVGAETFYVDGA RT(426–445)

Possible HLA

A34	A*3401,A*3402
A74	A*7401,A*7402
B53	B*5301
B81	B*8101
Cw4	C4,Cw*0401,C*0401,Cw*0402
Cw8	Cw*08,Cw*0801,Cw*0802,C*0802,Cw*0803

Possible Epitopes based on anchor residues

(7-16)	EPIVGAETFY	B*5301
(7-15)	EPIVGAETF	Cw*0401

Anchor Residues Searched

B*5301	X[P]XXXXXX[LIVMY]
B*5301	X[P]XXXXX[LIVMY]
B*5301	X[P]XXXXXXX[LIVMY]
Cw*0401	X[YPF]XXXXXX[LF]
Cw*0401	X[YPF]XXXXX[LF]
Cw*0401	X[YPF]XXXXXXX[LF]

This table lists epitopes that are experimentally observed to be presented by a HLA type carried by the patient, but the de£ned epitope has substitutions relative to the peptides from your reference strains and so might be missed by your reagents: in HXB2 for Gag, Pol; MN for Env; BRU for Nef, relative to most B clade Sequences in the database:

Protein	Epitope in Database	Epitope in Ref. strain	Epitope in Consensus B	HLA	Notes
p24(47–56)	ATPQDLNMML	ATPQDLNTML	ATPQDLNTML	B53	
p24(48–56)	TPYDINQML	TPQDLNTML	TPQDLNTML	B*5301	
p24(48–56)	TPQDLNQML	TPQDLNTML	TPQDLNTML	B53	
p24(48–56)	TPYDINQML	TPQDLNTML	TPQDLNTML	B53	
Protease(3–11)	ITLWQRPLV	VTLWQRPLV	ITLWQRPLV	A*6802,A*7401,A19	
Protease(3–11)	ITLWQRPLV	VTLWQRPLV	ITLWQRPLV	A*7401	
gp160(156–165)	NCSFNISTSI	NCSFNITTSI	NCSFNITTSI	Cw*08	
gp160(156–165)	NCSFNISTSI	NCSFNITTSI	NCSFNITTSI	Cw8	
gp160(239–247)	CTNVSTVQC	CKNVSTVQC	CTNVSTVQC	Cw8	
Nef(73–82)	SVPLRPMTYK	QVPLRPMTYK	QVPLRPMTYK	B35 or C4	

Table 1: **p24**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(47–56)	p24()	ATPQDLNMML	HIV-1 exposed seronegative	human(B53)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-speci£c CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
p24(48–56)	Gag(173–181 HIV-2)	TPYDINQML	HIV-2	human(B*5301)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*5301 epitope				
p24(48–56)	p24()	TPQDLNQML		human(B53)	[Rowland-Jones (1999)]
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: TPYDINQML, no cross-reactivity, [Gotch (1993)]				
p24(48–56)	Gag(173–181 HIV-2)	TPYDINQML	HIV-2	human(B53)	[Gotch (1993)]

Table 2: **Protease**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Protease(3–11)	Protease(71–79 LAI)	ITLWQRPLV		human(A*6802,A*7401,A*09)	[Ding (1998)]
	• Predicted on binding motif, no truncations analyzed • Clade A/B/D consensus, S. Rowland-Jones, pers. comm.				
Protease(3–11)	RT(71–79 A/B/D)	ITLWQRPLV	?	human(A*7401)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*7401 epitope				

Table 3: **gp160**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(156–165)	gp120(156–165)	NCSFNISTSI	HIV-1 infection	human(Cw*08)	[Ferris (1999)]
	• Recognized by CTL clone LWF A5, isolated from a lab worker exposed to HIV-1 in 1985 • The processing of this epitope is TAP1/2-dependent, as are most Env epitopes, and it contains two N-linked glycosylation sites that are glycosylated in Env • Only peptide that has been deglycosylated, a process that changes asparagine (N) to aspartic acid (D) was recognized: the aspartic acid at position 5 was critical, position 1 could be either D or N • This peptide also contains a Cys involved in a disul£de linkage but reducing conditions did not effect recognition by CTL clone LWF A5 • The HIV-1 Env epitopes are typically processed by a TAP1/2 dependent mechanism, which involves cotranslational translocation into the ER, glycosylation, export back into the cytosol, and deglycosylation for processing, and retransport into the ER for the association with class I molecules • The particular pathway of generating an epitope may have an impact on the presentation of that epitope, quantitatively as well as qualitatively				
gp160(156–165)	gp120(156–165 IIIB)	NCSFNISTSI	HIV-1 infection	human(Cw8)	[Sipsas (1997)]
	• HIV IIIB proteins were used to de£ne the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • NCSFNITTSI, a variant found in HIV-1 MN, was not recognized, thus this epitope was type-speci£c • NCSFNISTSI contains two potential N-linked glycosylation sites and cysteine residue, possibly related to the requirement for a high sensitizing dose of peptide for CTL activity				
gp160(239–247)	gp120(241–249 LAI)	CTNVSTVQC	HIV-1 infection	human(Cw8)	[Sipsas (1997)]
	• HIV IIIB proteins were used to de£ne the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • CTNVSTVQC contains a potential N-linked glycosylation site and cysteine residues, possibly related to a requirement for a high sensitizing dose of peptide for CTL activity				

Table 4: **Nef**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82 LAI)	SVPLRPMTYK	HIV-1 infection	human(B35 or C4)	[Buseyne (1993)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in £ve children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				

Table 5: **All De£ned Epitopes within the 20mer, regardless of HLA type**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(72–79)	Nef()	VPLRPMTY	HIV-1 exposed seronegative	human(B35)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-speci£c CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Nef(72–79)	Nef()	VPLRPMTY	HIV-1 infection	human(B35)	[Wilson (2000)]
	• Three individuals with highly focused HIV-speci£c CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-speci£c CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-speci£c T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been de£ned earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(72–91)	Nef(71–90 SF2)	PQVPLRMTYKAAVDLSHFL	HIV-1 infection	human()	[Lieberman (1997a)]
	• Of 25 patients, most had CTL speci£c for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A3, A32, B51, B62; HLA-A11, A24, B8, B53				
Nef(72–91)	Nef(71–90 SF2)	PQVPLRPMTYKAAVDLSHFL	HIV-1 infection	human()	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV infection	human()	[Garcia (1997)]
	• The anti-Nef CTL line P1 speci£c for this epitope is able to kill target cells via two mechanisms • First: Ca^{2+}-dependent, perforin-dependent Nef-speci£c lysis • Second: Ca^{2+}-independent, CD95-dependent apoptosis that could also kill non-speci£c targets • Findings indicate that the two mechanisms are not mutually exclusive in human CTL, as they are in mice • CTL mediated CD95-dependent apoptosis may play a role in pathogenesis				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82 NL43)	QVPLRPMTYK	HIV-1 infection	human(A*0301)	[Koenig (1990)]
	• 81 Tyr is critical for binding to A3.1 • C. Brander notes that this is an A*0301 epitope in the 1999 database				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK		human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Le Borgne (2000)]
	• Soluble factors in supernatant from both an HIV-speci£c cloned CTL line and an EBV (Epstein-Barr-virus) CTL line inhibit viral replication, but do not block viral entry in CD4+ T lymphocytes, by a noncytotoxic mechanism				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Robertson (1993)]
	• Development of a retroviral vector (pNeoNef) to generate autologous CTL targets • [Hunziker (1998)] suggests that HLA-A2 does not in fact present this epitope • The initial assignment of HLA-A2 presentation for this epitope was based on a serological HLA typing. Subsequently, the authors revisited the issue with genetic HLA typing and found that HLA-A11 was the correct presenting molecule (Dr. Florence Buseyne, Pers. Comm., 2000)				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin (1994), Goulder (1997a)]
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin (1995)]
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				
Nef(73–82)	()	QVPLRPMTYK		(A11)	[Brander & Goulder(2001), Buseyne(1999)]
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-infection	human(A3)	[Chassin (1999)]
	• Mutations in Nef that ¤ank this epitope, Thr71Lys and Ala83Gly, may account for an observed loss of CTL reactivity, with escape due to the introduction of proteasome processing defects				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Durali (1998)]
	• Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • One of the patients was shown to react to this epitope: QVPLRPMTYK			
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Goulder (1997b), Goulder (1997a)]
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • Both had a response to this epitope • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Lubaki (1997)]
	• Eighty two HIV-1-speci£c CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • An A3+ subject had a strong response to this epitope, with 10/11 CTL clones being speci£c for this epitope, isolated at two time points, 1 year apart				
Nef(73–82)	Nef(73–82 BRU)	QVPLRPMTYK	HIV-1 infection	human(A3, A11, B35)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Koenig (1995)]
	• Alanine substitutions L76A, R77A, M79A, T80A signi£cantly decreased immunogenicity of peptide • Nef CTL clones (4N225) were infused into an HIV-1 infected volunteer to evaluate effects of infusion on viral load/patient health • Infusion led to outburst of escape variants which resulted in higher viral load/accelerated disease progression				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty £ve optimally de£ned peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals was A3, and responded to QVPLRPMTYK as well as two other A3.1 epitopes				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(B*0301)	[Wilson (2000)]
	• Three individuals with highly focused HIV-speci£c CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-speci£c CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-speci£c T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been de£ned earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK		human(B27)	[Culmann(1998)]
	• Optimal epitope mapped by peptide titration				
Nef(73–82)	Nef(73–82 LAI)	SVPLRPMTYK	HIV-1 infection	human(B35 or C4)	[Buseyne (1993)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in £ve children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef(74–81)	Nef(74–82)	VPLRPMTY		human(A3)	[Carreno (1992)]
	• Included in HLA-A3 binding peptide competition study				
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
Nef(74–81)	Nef(75–82)	VPLRPMTY	no CTL shown	human(B*3501)	[Smith (1996)]
	• Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex				
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B35)	[McMichael & Walker(1994), Culmann (1991)]
	• Review of HIV CTL epitopes – de£ned by B35 motif found within a larger peptide				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or -2 infection	human(B35)	[Rowland-Jones (1995)]
	• VPLRPMTY also recognized by CTL from HIV-2 seropositives; epitope is conserved				
Nef(74–81)	Nef()	VPLRPMTY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998a)]
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-de£ned B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A and D subtype consensus are identical to the B clade epitope				
Nef(74–81)	Nef(75–82)	VPLRPMTY	none	human(B35)	[Lalvani (1997)]
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-speci£c CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors				
Nef(74–81)	Nef()	VPLRPMTY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998b)]
	• HIV-speci£c CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B, and D clade viruses				
Nef(74–81)	Nef()	VPLRPMTY		human(B35)	[Rowland-Jones (1999)]
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, • HIV-2 version of this epitope is conserved: VPLRPMTY, and CTLs are cross-reactive – one of £ve B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]				
Nef(74–82)	Nef(73–82)	VPLRPMTYK	no CTL shown	human(A11)	[Zhang (1993)]
	• Exploration of A11 binding motif				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(75–82)	Nef(75–82 LAI)	PLRPMTYK	HIV-1 infection	human(A*1101)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • C. Brander notes that this is an A*1101 epitope in the 1999 database				
Nef(75–82)	Nef(75–82 LAI)	PLRPMTYK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*1101 epitope				
Nef(77–85)	Nef(77–85 LAI)	RPMTYKAAL	HIV-1 infection	human(B*0702)	[Bauer (1997)]
	• Structural constraints on the Nef protein may prevent escape • Noted in Brander 1999, this database, to be B*0702				
Nef(77–85)	Nef(77–85 LAI)	RPMTYKAAL	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
Nef(82–91)	Nef(82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human(C*0802)	[Nixon (1999)]
	• A patient who made a mono-speci£c CTL response to this Nef speci£c epitope was given effective anti-retroviral therapy within 90 days of infection, reducing the antigenic stimulous • Within 7 days of therapy, his CTLp frequency dropped from 60 to 4 per million PBMC, as his viremia dropped • The patient went from having an activated effector population (detected by CTLp and clone speci£c RNA) to a non-activated quiescent population (detected by the CTL-clone speci£c DNA)				
Nef(82–91)	Nef(82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human(C*0802(Cw8))	[Brander & Goulder(2001)]
	• C. Brander notes this is a C*0802(Cw8) epitope				
Nef(84–91)	Nef(84–91 LAI)	AVDLSHFL	HIV-1 infection	human(Bw62)	[Culmann-Penciolelli (1994)]
Nef(84–91)	Nef(84–91)	AVDLSHFL	HIV-1 infection	human(Bw62)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty £ve optimally de£ned peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals that didn„t respond to SLYNTVATL reacted with seven other epitopes including this epitope				

Table 6: **All De£ned Epitopes within the 20mer, regardless of HLA type**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(72–79)	Nef()	VPLRPMTY	HIV-1 exposed seronegative	human(B35)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-speci£c CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Nef(72–79)	Nef()	VPLRPMTY	HIV-1 infection	human(B35)	[Wilson (2000)]
	• Three individuals with highly focused HIV-speci£c CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-speci£c CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-speci£c T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been de£ned earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(72–91)	Nef(71–90 SF2)	PQVPLRMTYKAAVDLSHFL	HIV-1 infection	human()	[Lieberman (1997a)]
	• Of 25 patients, most had CTL speci£c for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A3, A32, B51, B62; HLA-A11, A24, B8, B53				
Nef(72–91)	Nef(71–90 SF2)	PQVPLRPMTYKAAVDLSHFL	HIV-1 infection	human()	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV infection	human()	[Garcia (1997)]
	• The anti-Nef CTL line P1 speci£c for this epitope is able to kill target cells via two mechanisms • First: Ca^{2+}-dependent, perforin-dependent Nef-speci£c lysis • Second: Ca^{2+}-independent, CD95-dependent apoptosis that could also kill non-speci£c targets • Findings indicate that the two mechanisms are not mutually exclusive in human CTL, as they are in mice • CTL mediated CD95-dependent apoptosis may play a role in pathogenesis				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82 NL43)	QVPLRPMTYK	HIV-1 infection	human(A*0301)	[Koenig (1990)]
	• 81 Tyr is critical for binding to A3.1 • C. Brander notes that this is an A*0301 epitope in the 1999 database				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK		human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Le Borgne (2000)]
	• Soluble factors in supernatant from both an HIV-speci£c cloned CTL line and an EBV (Epstein-Barr-virus) CTL line inhibit viral replication, but do not block viral entry in CD4+ T lymphocytes, by a noncytotoxic mechanism				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Robertson (1993)]
	• Development of a retroviral vector (pNeoNef) to generate autologous CTL targets • [Hunziker (1998)] suggests that HLA-A2 does not in fact present this epitope • The initial assignment of HLA-A2 presentation for this epitope was based on a serological HLA typing. Subsequently, the authors revisited the issue with genetic HLA typing and found that HLA-A11 was the correct presenting molecule (Dr. Florence Buseyne, Pers. Comm., 2000)				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin (1994), Goulder (1997a)]
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin (1995)]
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				
Nef(73–82)	()	QVPLRPMTYK		(A11)	[Brander & Goulder(2001), Buseyne(1999)]
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-infection	human(A3)	[Chassin (1999)]
	• Mutations in Nef that ¤ank this epitope, Thr71Lys and Ala83Gly, may account for an observed loss of CTL reactivity, with escape due to the introduction of proteasome processing defects				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Durali (1998)]
	• Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • One of the patients was shown to react to this epitope: QVPLRPMTYK			
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Goulder (1997b), Goulder (1997a)]
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • Both had a response to this epitope • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Lubaki (1997)]
	• Eighty two HIV-1-speci£c CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • An A3+ subject had a strong response to this epitope, with 10/11 CTL clones being speci£c for this epitope, isolated at two time points, 1 year apart				
Nef(73–82)	Nef(73–82 BRU)	QVPLRPMTYK	HIV-1 infection	human(A3, A11, B35)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Koenig (1995)]
	• Alanine substitutions L76A, R77A, M79A, T80A signi£cantly decreased immunogenicity of peptide • Nef CTL clones (4N225) were infused into an HIV-1 infected volunteer to evaluate effects of infusion on viral load/patient health • Infusion led to outburst of escape variants which resulted in higher viral load/accelerated disease progression				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty £ve optimally de£ned peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals was A3, and responded to QVPLRPMTYK as well as two other A3.1 epitopes				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(B*0301)	[Wilson (2000)]
	• Three individuals with highly focused HIV-speci£c CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-speci£c CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-speci£c T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been de£ned earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK		human(B27)	[Culmann(1998)]
	• Optimal epitope mapped by peptide titration				
Nef(73–82)	Nef(73–82 LAI)	SVPLRPMTYK	HIV-1 infection	human(B35 or C4)	[Buseyne (1993)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in £ve children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef(74–81)	Nef(74–82)	VPLRPMTY		human(A3)	[Carreno (1992)]
	• Included in HLA-A3 binding peptide competition study				
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
Nef(74–81)	Nef(75–82)	VPLRPMTY	no CTL shown	human(B*3501)	[Smith (1996)]
	• Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex				
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B35)	[McMichael & Walker(1994), Culmann (1991)]
	• Review of HIV CTL epitopes – de£ned by B35 motif found within a larger peptide				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or -2 infection	human(B35)	[Rowland-Jones (1995)]
	• VPLRPMTY also recognized by CTL from HIV-2 seropositives; epitope is conserved				
Nef(74–81)	Nef()	VPLRPMTY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998a)]
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-de£ned B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A and D subtype consensus are identical to the B clade epitope				
Nef(74–81)	Nef(75–82)	VPLRPMTY	none	human(B35)	[Lalvani (1997)]
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-speci£c CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors				
Nef(74–81)	Nef()	VPLRPMTY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998b)]
	• HIV-speci£c CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B, and D clade viruses				
Nef(74–81)	Nef()	VPLRPMTY		human(B35)	[Rowland-Jones (1999)]
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, • HIV-2 version of this epitope is conserved: VPLRPMTY, and CTLs are cross-reactive – one of £ve B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]				
Nef(74–82)	Nef(73–82)	VPLRPMTYK	no CTL shown	human(A11)	[Zhang (1993)]
	• Exploration of A11 binding motif				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(75–82)	Nef(75–82 LAI)	PLRPMTYK	HIV-1 infection	human(A*1101)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • C. Brander notes that this is an A*1101 epitope in the 1999 database				
Nef(75–82)	Nef(75–82 LAI)	PLRPMTYK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*1101 epitope				
Nef(77–85)	Nef(77–85 LAI)	RPMTYKAAL	HIV-1 infection	human(B*0702)	[Bauer (1997)]
	• Structural constraints on the Nef protein may prevent escape • Noted in Brander 1999, this database, to be B*0702				
Nef(77–85)	Nef(77–85 LAI)	RPMTYKAAL	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
Nef(82–91)	Nef(82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human(C*0802)	[Nixon (1999)]
	• A patient who made a mono-speci£c CTL response to this Nef speci£c epitope was given effective anti-retroviral therapy within 90 days of infection, reducing the antigenic stimulous • Within 7 days of therapy, his CTLp frequency dropped from 60 to 4 per million PBMC, as his viremia dropped • The patient went from having an activated effector population (detected by CTLp and clone speci£c RNA) to a non-activated quiescent population (detected by the CTL-clone speci£c DNA)				
Nef(82–91)	Nef(82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human(C*0802(Cw8))	[Brander & Goulder(2001)]
	• C. Brander notes this is a C*0802(Cw8) epitope				
Nef(84–91)	Nef(84–91 LAI)	AVDLSHFL	HIV-1 infection	human(Bw62)	[Culmann-Penciolelli (1994)]
Nef(84–91)	Nef(84–91)	AVDLSHFL	HIV-1 infection	human(Bw62)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty £ve optimally de£ned peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals that didn„t respond to SLYNTVATL reacted with seven other epitopes including this epitope				

Table 7: **All De£ned Epitopes within the 20mer, regardless of HLA type**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(72–79)	Nef()	VPLRPMTY	HIV-1 exposed seronegative	human(B35)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-speci£c CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
Nef(72–79)	Nef()	VPLRPMTY	HIV-1 infection	human(B35)	[Wilson (2000)]
	• Three individuals with highly focused HIV-speci£c CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-speci£c CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-speci£c T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been de£ned earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(72–91)	Nef(71–90 SF2)	PQVPLRMTYKAAVDLSHFL	HIV-1 infection	human()	[Lieberman (1997a)]
	• Of 25 patients, most had CTL speci£c for more than 1 HIV-1 protein • Eleven subjects had CTL that could recognize vaccinia-expressed LAI Nef • Three of these 11 had CTL response to this peptide • The responding subjects were HLA-A3, A32, B51, B62; HLA-A11, A24, B8, B53				
Nef(72–91)	Nef(71–90 SF2)	PQVPLRPMTYKAAVDLSHFL	HIV-1 infection	human()	[Lieberman (1997b)]
	• CTL expanded *ex vivo* were later infused into HIV-1 infected patients				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV infection	human()	[Garcia (1997)]
	• The anti-Nef CTL line P1 speci£c for this epitope is able to kill target cells via two mechanisms • First: Ca^{2+}-dependent, perforin-dependent Nef-speci£c lysis • Second: Ca^{2+}-independent, CD95-dependent apoptosis that could also kill non-speci£c targets • Findings indicate that the two mechanisms are not mutually exclusive in human CTL, as they are in mice • CTL mediated CD95-dependent apoptosis may play a role in pathogenesis				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82 NL43)	QVPLRPMTYK	HIV-1 infection	human(A*0301)	[Koenig (1990)]
	• 81 Tyr is critical for binding to A3.1 • C. Brander notes that this is an A*0301 epitope in the 1999 database				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK		human(A*0301)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*0301 epitope				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Le Borgne (2000)]
	• Soluble factors in supernatant from both an HIV-speci£c cloned CTL line and an EBV (Epstein-Barr-virus) CTL line inhibit viral replication, but do not block viral entry in CD4+ T lymphocytes, by a noncytotoxic mechanism				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Robertson (1993)]
	• Development of a retroviral vector (pNeoNef) to generate autologous CTL targets • [Hunziker (1998)] suggests that HLA-A2 does not in fact present this epitope • The initial assignment of HLA-A2 presentation for this epitope was based on a serological HLA typing. Subsequently, the authors revisited the issue with genetic HLA typing and found that HLA-A11 was the correct presenting molecule (Dr. Florence Buseyne, Pers. Comm., 2000)				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin (1994), Goulder (1997a)]
	• Mutational variation in HIV epitopes in individuals with appropriate HLA types can result in evasion of CTL response • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A11)	[Couillin (1995)]
	• Mutations found in this epitope in HLA-A11 positive and negative donors were characterized				
Nef(73–82)	()	QVPLRPMTYK		(A11)	[Brander & Goulder(2001), Buseyne(1999)]
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-infection	human(A3)	[Chassin (1999)]
	• Mutations in Nef that ¤ank this epitope, Thr71Lys and Ala83Gly, may account for an observed loss of CTL reactivity, with escape due to the introduction of proteasome processing defects				

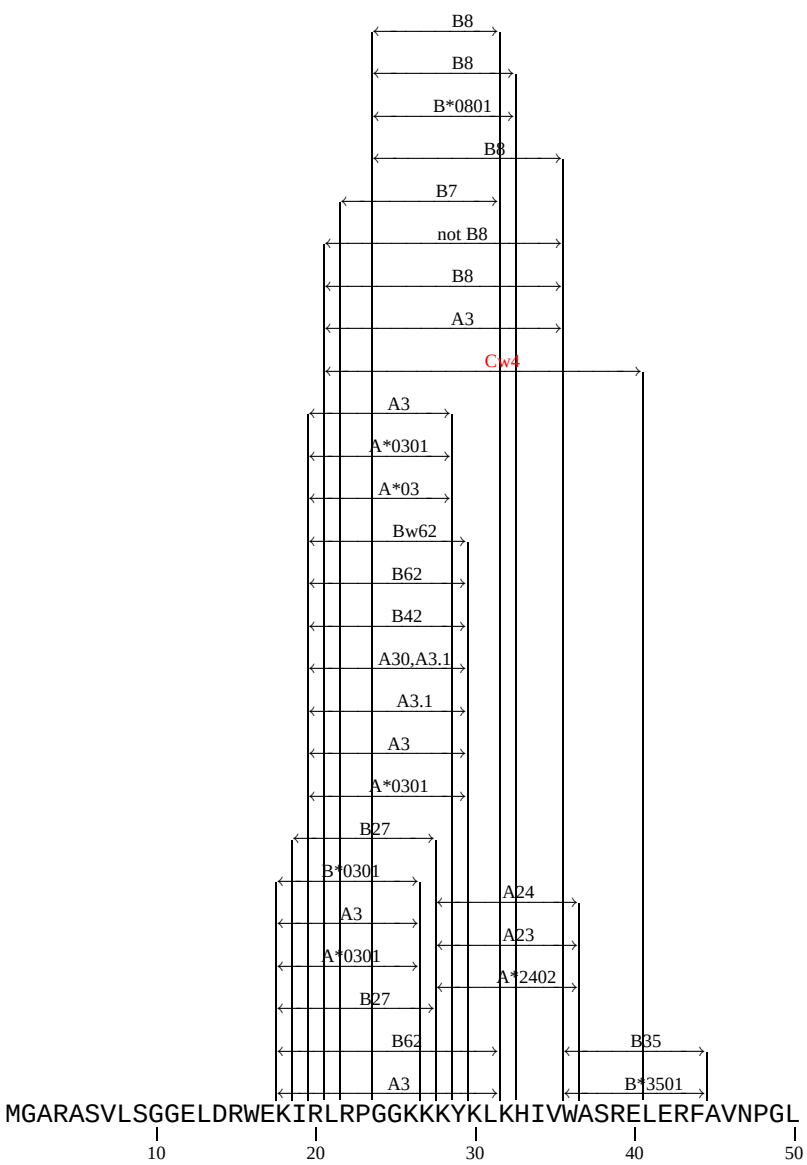
HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Durali (1998)]
	• Cross-clade CTL response was studied by determining the CTL activity in seven patients from Bangui, (6 A subtype, and 1 AG recombinant infections) and one A subtype infection from a person living in France originally from Togo, to different antigens expressed in vaccinia • Pol reactivity: 8/8 had CTL to A subtype, and 7/8 to B subtype, and HIV-2 Pol was not tested • Gag reactivity: 7/8 reacted with A or B subtype gag, 3/8 with HIV-2 Gag • Nef reactivity: 7/8 reacted with A subtype, and 5/8 with B subtype, none with HIV-2 Nef • Env reactivity: 3/8 reacted with A subtype, 1/8 with B subtype, none with HIV-2 Env • One of the patients was shown to react to this epitope: QVPLRPMTYK			
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Goulder (1997b), Goulder (1997a)]
	• Identical twin hemophiliac brothers were both infected with the same batch of factor VIII • Both had a response to this epitope • [Goulder (1997a)] is a review of immune escape that summarizes this study				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3)	[Lubaki (1997)]
	• Eighty two HIV-1-speci£c CTL clones from 5 long-term non-progressors were isolated and analyzed for breadth of response • A sustained Gag, Env and Nef response was observed, and clones were restricted by multiple HLA epitopes, indicating a polyclonal response • An A3+ subject had a strong response to this epitope, with 10/11 CTL clones being speci£c for this epitope, isolated at two time points, 1 year apart				
Nef(73–82)	Nef(73–82 BRU)	QVPLRPMTYK	HIV-1 infection	human(A3, A11, B35)	[Culmann (1991)]
	• Nef CTL clones from HIV+ donors				
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Koenig (1995)]
	• Alanine substitutions L76A, R77A, M79A, T80A signi£cantly decreased immunogenicity of peptide • Nef CTL clones (4N225) were infused into an HIV-1 infected volunteer to evaluate effects of infusion on viral load/patient health • Infusion led to outburst of escape variants which resulted in higher viral load/accelerated disease progression				
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(A3.1)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty £ve optimally de£ned peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals was A3, and responded to QVPLRPMTYK as well as two other A3.1 epitopes				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(73–82)	Nef(73–82)	QVPLRPMTYK	HIV-1 infection	human(B*0301)	[Wilson (2000)]
	• Three individuals with highly focused HIV-speci£c CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-speci£c CD8+ T cells were found prior to seroconversion, and there was a close temporal relationship between the number of circulating HIV-speci£c T cells and viral load was also found • All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B2705; and A*0201, A*0301, B2705, B39 • ELISPOT was used to test a panel of CTL epitopes that had been de£ned earlier and were appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK • The subject with A*0201 had a moderatly strong response to SLYNTVATL • Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705 • No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL			
Nef(73–82)	Nef(73–82 LAI)	QVPLRPMTYK		human(B27)	[Culmann(1998)]
	• Optimal epitope mapped by peptide titration				
Nef(73–82)	Nef(73–82 LAI)	SVPLRPMTYK	HIV-1 infection	human(B35 or C4)	[Buseyne (1993)]
	• Vertical transmission of HIV ranges from 13% to 39% • Primary assays showed cytotoxic activity against at least one HIV protein was detected in 70% of infected children • Epitopes recognized in £ve children were mapped using synthetic peptides and secondary cultures • Patient EM13, who had a CTL response to three epitopes in Nef, was infected via blood transfusion after birth and went from CDC stage P2A to P2E during the study				
Nef(74–81)	Nef(74–82)	VPLRPMTY		human(A3)	[Carreno (1992)]
	• Included in HLA-A3 binding peptide competition study				
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B*3501)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*3501 epitope				
Nef(74–81)	Nef(75–82)	VPLRPMTY	no CTL shown	human(B*3501)	[Smith (1996)]
	• Crystal structure of VPLRPMTY-class I B allele HLA-B*3501 complex				
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or HIV-2 infection	human(B35)	[McMichael & Walker(1994), Culmann (1991)]
	• Review of HIV CTL epitopes – de£ned by B35 motif found within a larger peptide				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(74–81)	Nef(73–82 LAI)	VPLRPMTY	HIV-1 or -2 infection	human(B35)	[Rowland-Jones (1995)]
	• VPLRPMTY also recognized by CTL from HIV-2 seropositives; epitope is conserved				
Nef(74–81)	Nef()	VPLRPMTY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998a)]
	• A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-de£ned B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating • The A and D subtype consensus are identical to the B clade epitope				
Nef(74–81)	Nef(75–82)	VPLRPMTY	none	human(B35)	[Lalvani (1997)]
	• A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-speci£c CTLp counts could be obtained via staining with peptide-Class I tetramers • This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors				
Nef(74–81)	Nef()	VPLRPMTY	HIV-1 exposure	human(B35)	[Rowland-Jones (1998b)]
	• HIV-speci£c CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B, and D clade viruses				
Nef(74–81)	Nef()	VPLRPMTY		human(B35)	[Rowland-Jones (1999)]
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, • HIV-2 version of this epitope is conserved: VPLRPMTY, and CTLs are cross-reactive – one of £ve B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]				
Nef(74–82)	Nef(73–82)	VPLRPMTYK	no CTL shown	human(A11)	[Zhang (1993)]
	• Exploration of A11 binding motif				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Nef(75–82)	Nef(75–82 LAI)	PLRPMTYK	HIV-1 infection	human(A*1101)	[McMichael & Walker(1994)]
	• Review of HIV CTL epitopes • C. Brander notes that this is an A*1101 epitope in the 1999 database				
Nef(75–82)	Nef(75–82 LAI)	PLRPMTYK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*1101 epitope				
Nef(77–85)	Nef(77–85 LAI)	RPMTYKAAL	HIV-1 infection	human(B*0702)	[Bauer (1997)]
	• Structural constraints on the Nef protein may prevent escape • Noted in Brander 1999, this database, to be B*0702				
Nef(77–85)	Nef(77–85 LAI)	RPMTYKAAL	HIV-1 infection	human(B*0702)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0702 epitope				
Nef(82–91)	Nef(82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human(C*0802)	[Nixon (1999)]
	• A patient who made a mono-speci£c CTL response to this Nef speci£c epitope was given effective anti-retroviral therapy within 90 days of infection, reducing the antigenic stimulous • Within 7 days of therapy, his CTLp frequency dropped from 60 to 4 per million PBMC, as his viremia dropped • The patient went from having an activated effector population (detected by CTLp and clone speci£c RNA) to a non-activated quiescent population (detected by the CTL-clone speci£c DNA)				
Nef(82–91)	Nef(82–91 LAI)	KAAVDLSHFL	HIV-1 infection	human(C*0802(Cw8))	[Brander & Goulder(2001)]
	• C. Brander notes this is a C*0802(Cw8) epitope				
Nef(84–91)	Nef(84–91 LAI)	AVDLSHFL	HIV-1 infection	human(Bw62)	[Culmann-Penciolelli (1994)]
Nef(84–91)	Nef(84–91)	AVDLSHFL	HIV-1 infection	human(Bw62)	[Betts (2000)]
	• Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant • Ninty £ve optimally de£ned peptides from this database were used to screen for gamma interferon responses to other epitopes • 1/11 of the A2+ individuals that didn„t respond to SLYNTVATL reacted with seven other epitopes including this epitope				

p17 CTL Map


B8
B8
B*0801
B8
B7
not B8
B8
A3
Cw4
A3
A*0301
A*03
Bw62
B62
B42
A30,A3.1
A3.1
A3
A*0301
B27
B*0301
A3
A*0301
B27
B62
A3
A24
A23
A*2402
B35
B*3501
MGARASVLSGGELDRWEKIRLRPGGKKKYKLKHIVWASRELERFAVNPGL
10
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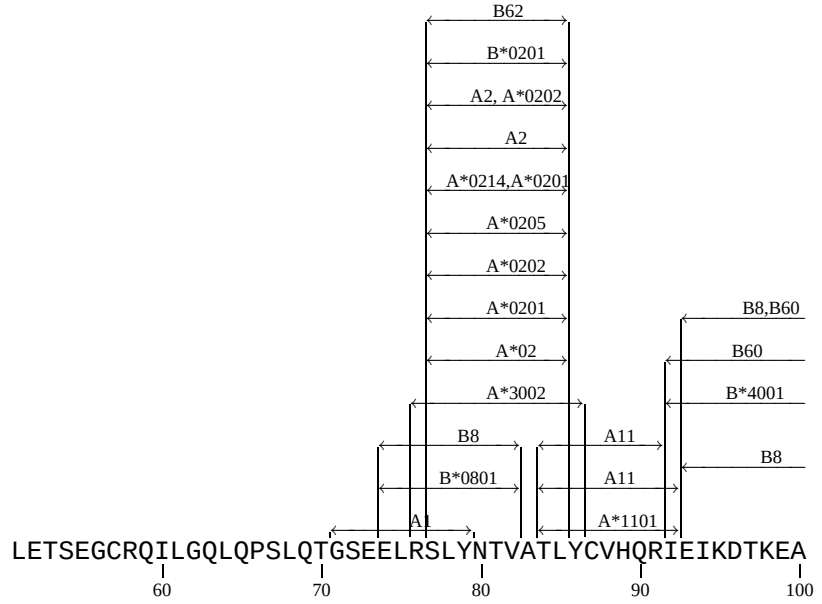
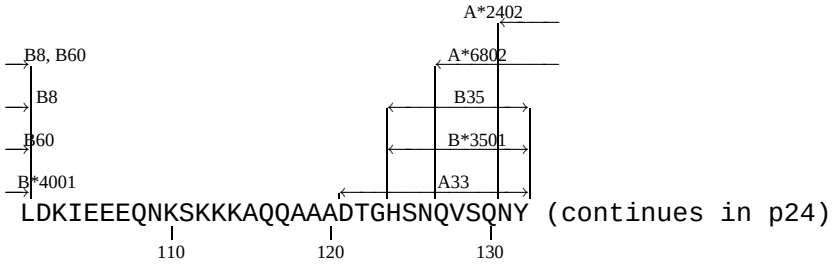
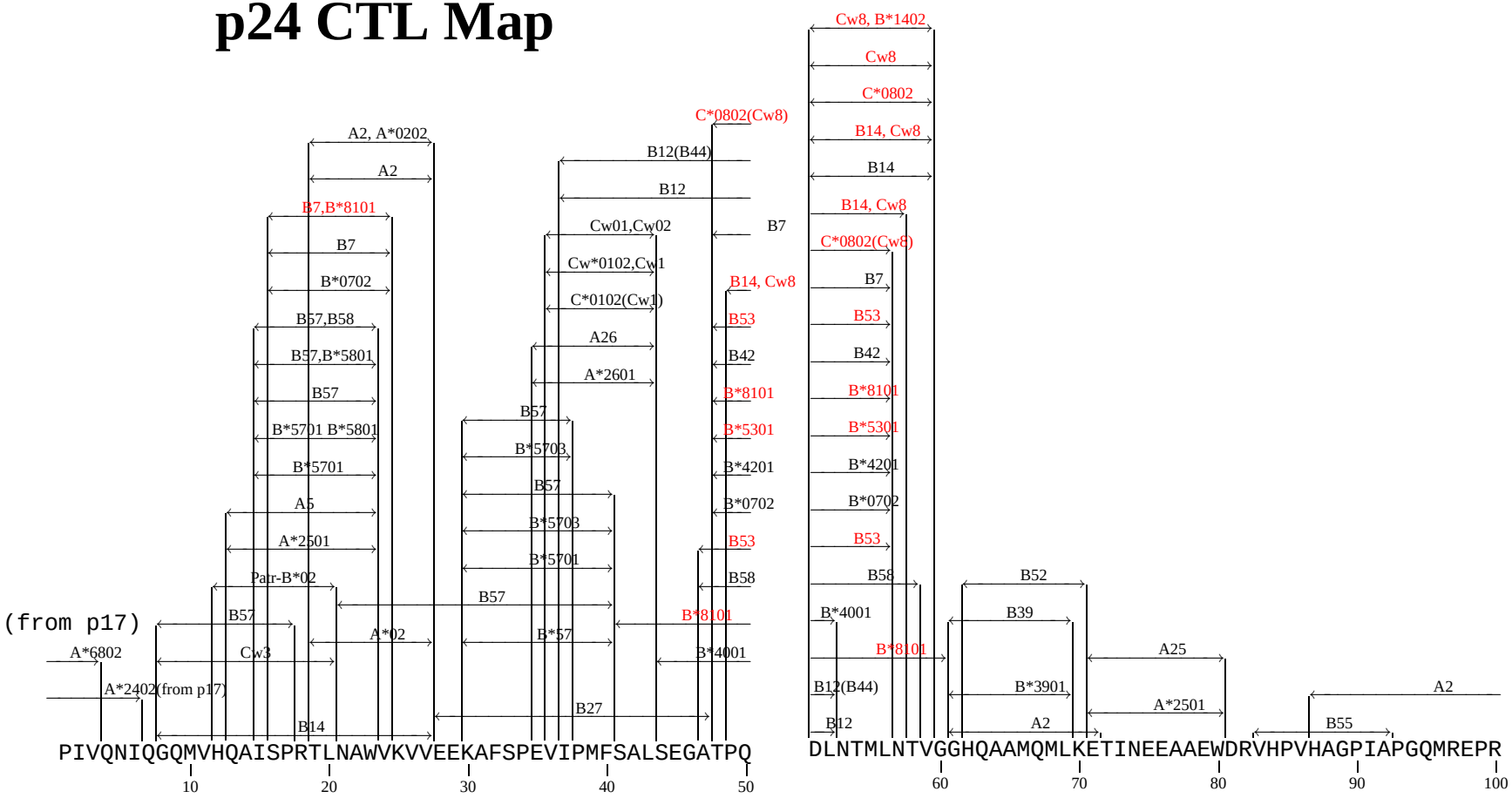
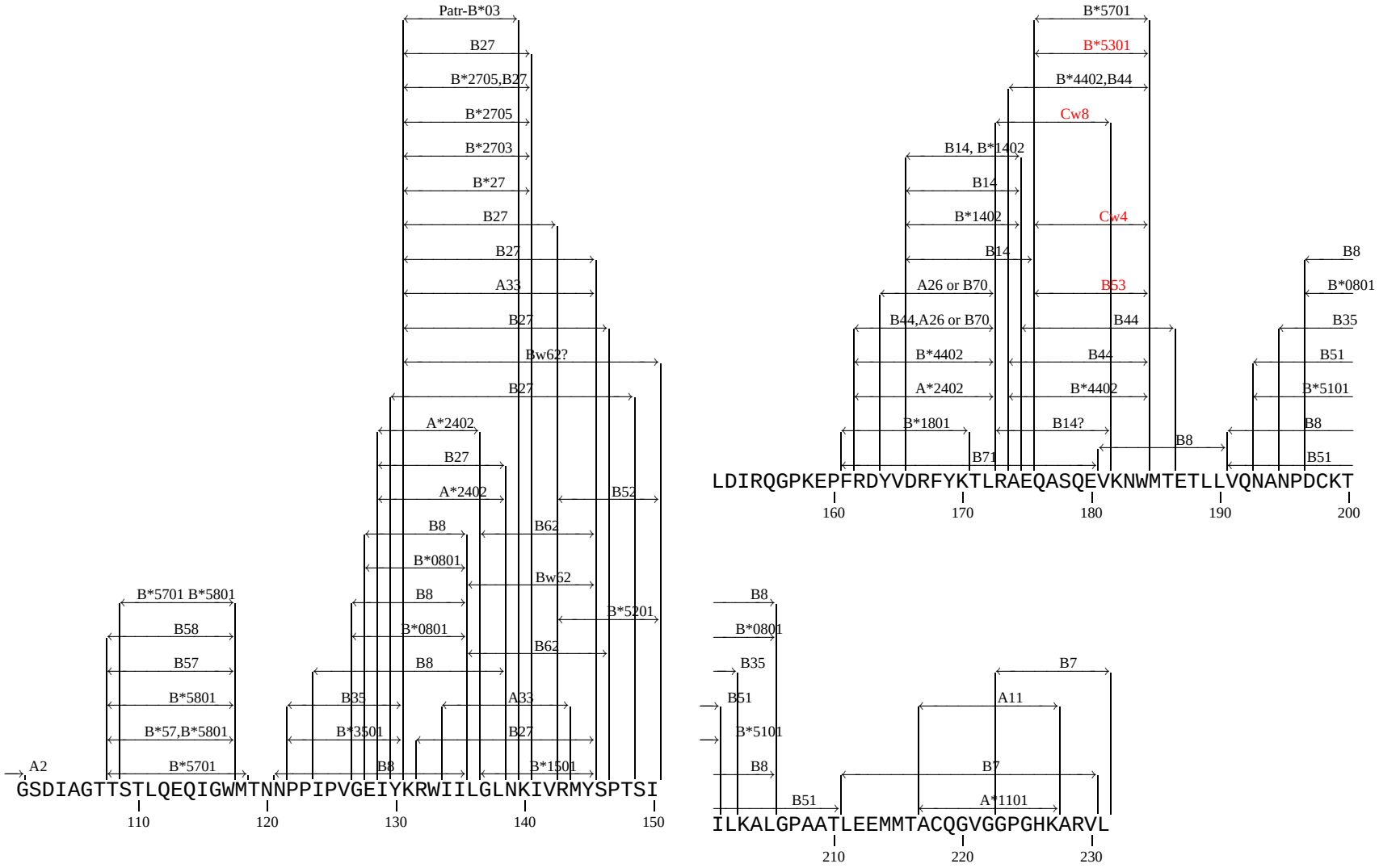
30
40
50


B62
B*0201
A2, A*0202
A2
A*0214,A*0201
A*0205
A*0202
A*0201
A*02
A*3002
B8
B*0801
A1
A11
A11
A*1101
B8,B60
B60
B*4001
B8
LETSEGCRQILGQLQPSLQTGSEELRSLYNTVATLYCVHQRIEIKDTKEA
60
70
80
90
100

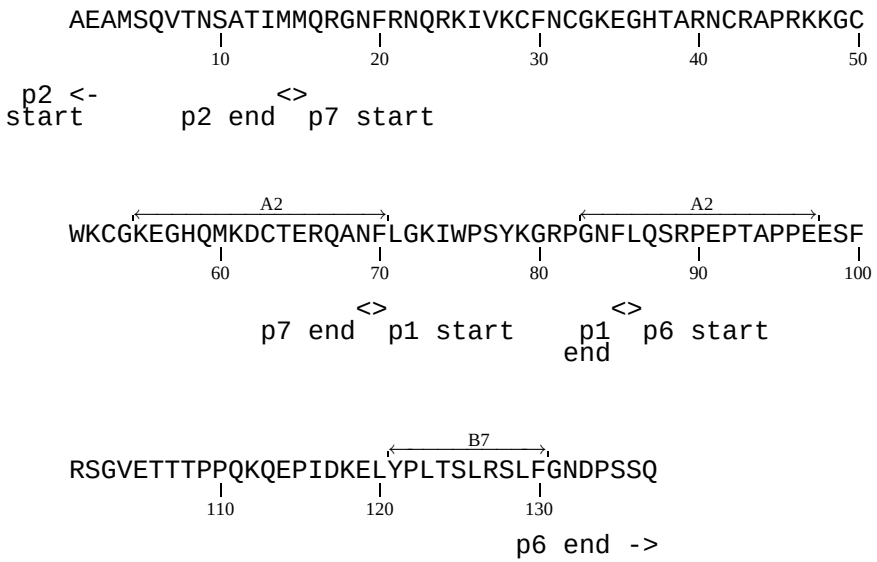

A*2402
A*6802
B35
B*3501
A33
B8, B60
B8
B60
B*4001
LDKIEEEQNKSKKKAQQAAADTGHSNQVSQNY (continues in p24)
110
120
130

p24 CTL Map

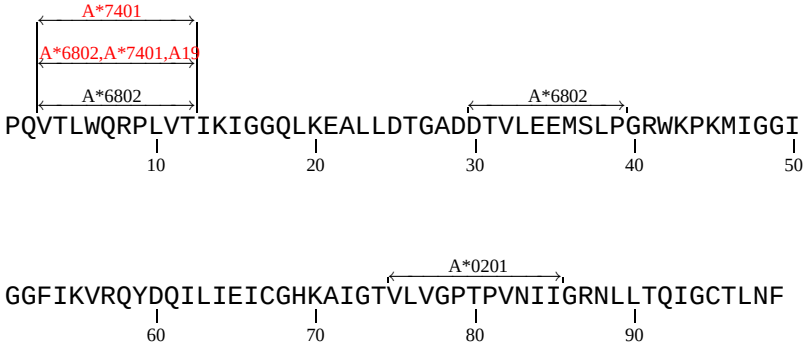

(from p17)
A*6802
A*2402(from p17)
A2, A*0202
A2
B7,B*8101
B7
B*0702
B57,B58
B57,B*5801
B57
B*5701 B*5801
B*5701
A5
A*2501
Pair-B*02
B57
A*02
Cw3
B14
C*0802(Cw8)
B12(B44)
B12
Cw01,Cw02
Cw*0102,Cw1
C*0102(Cw1)
A26
A*2601
B57
B*5703
B57
B*5703
B*5701
B57
B*57
B27
B7
B14, Cw8
B53
B42
B*8101
B*5301
B*4201
B*0702
B53
B58
B*8101
B*4001
PIVQNIQGQMVHQAISPRTLNAWVKVVEEKAFSPEVIPMFSALSEGATPQ
10
20
30
40
50
Cw8, B*1402
Cw8
C*0802
B14, Cw8
B14
B14, Cw8
C*0802(Cw8)
B7
B53
B42
B*8101
B*5301
B*4201
B*0702
B53
B58
B*4001
B*8101
B12(B44)
B12
B52
B39
A25
B*3901
A*2501
A2
A2
B55
DLNTMLNTVGGHQAAMQMLKETINEEAAEWDRVHPVHAGPIAPGQMREPR
60
70
80
90
100


Patr-B*03
B27
B*2705,B27
B*2705
B*2703
B*27
B27
B27
A33
B27
Bw62?
B27
A*2402
B27
A*2402
B52
B8
B62
B*0801
Bw62
B*5701 B*5801
B8
B*5201
B58
B*0801
B62
B57
B8
B*5801
B35
A33
B*57,B*5801
B*3501
B27
A2
B*5701
B8
B*1501
GSDIAGTTSTLQEQIGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSI
110
120
130
140
150
B*5701
B*5301
B*4402,B44
Cw8
B14, B*1402
B14
B*1402
Cw4
B14
B8
A26 or B70
B53
B*0801
B44,A26 or B70
B44
B35
B*4402
B44
B51
A*2402
B*4402
B*5101
B*1801
B14?
B8
B8
B71
B51
LDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQNANPDCKT
160
170
180
190
200
B8
B*0801
B35
B7
B51
A11
B*5101
B8
B7
B51
A*1101
ILKALGPAATLEEMMTACQGVGGPGHKARVL
210
220
230

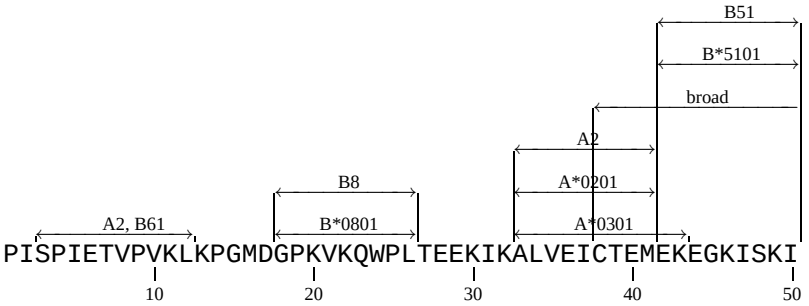
p2p7p1p6 CTL Map

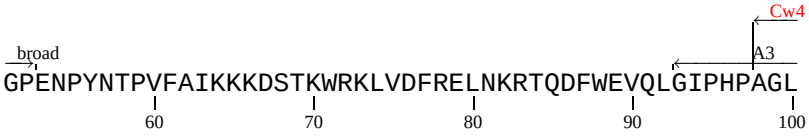


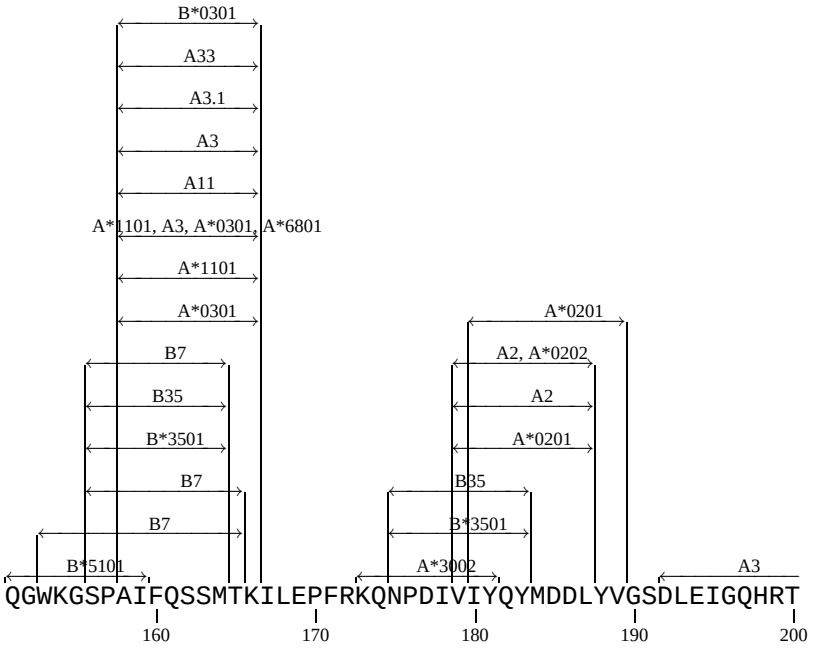
Protease CTL Map

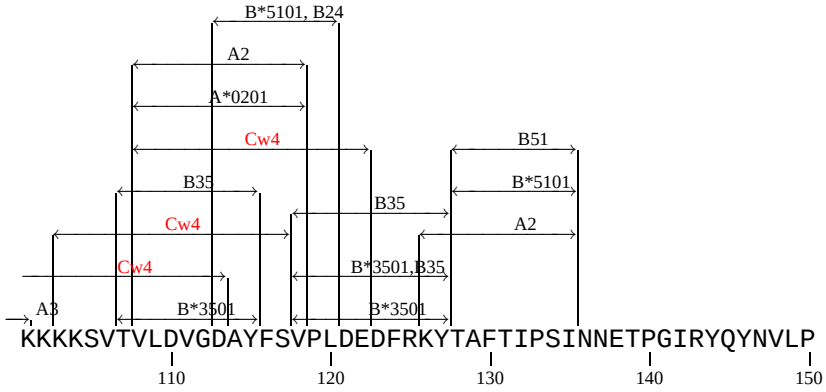


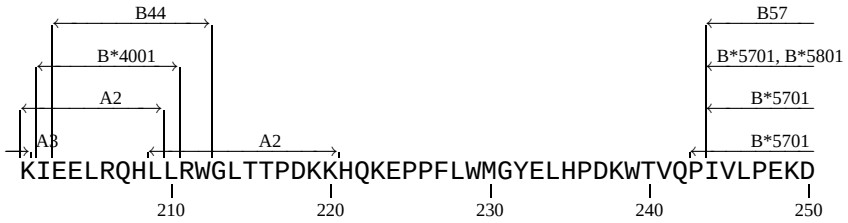
RT CTL Map

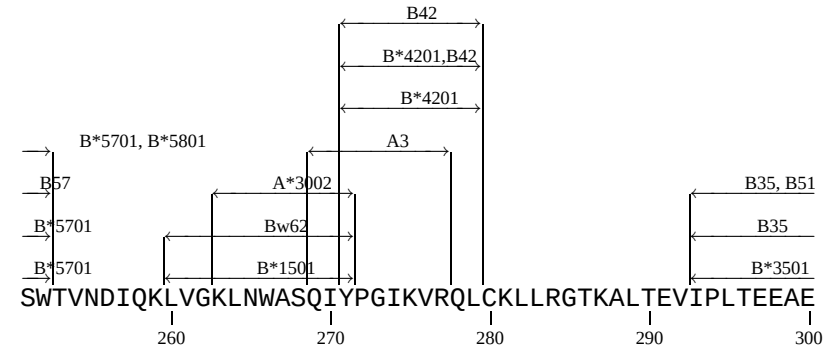

B51
B*5101
broad
A2
B8
A*0201
A2, B61
B*0801
A*0301
PISPIETVPVKLKPGMDGPKVKQWPLTEEKIKALVEICTEMEKEGKISKI
10
20
30
40
50

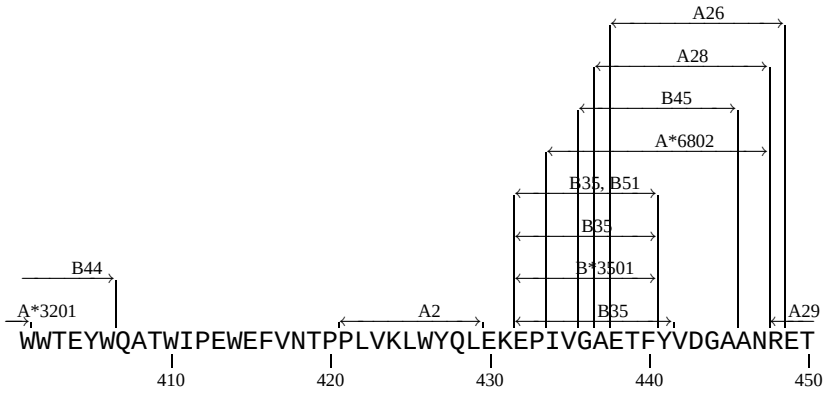

Cw4
broad
A3
GPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLGIPHPAGL
60
70
80
90
100


B*0301
A33
A3.1
A3
A11
A*1101, A3, A*0301, A*6801
A*1101
A*0301
B7
B35
B*3501
B7
B7
B*5101
A*0201
A2, A*0202
A2
A*0201
B35
B*3501
A*3002
A3
QGWKGSPAIFQSSMTKILEPFRKQNPDIVIYQYMDDLYVGSDLEIGQHRT
160
170
180
190
200

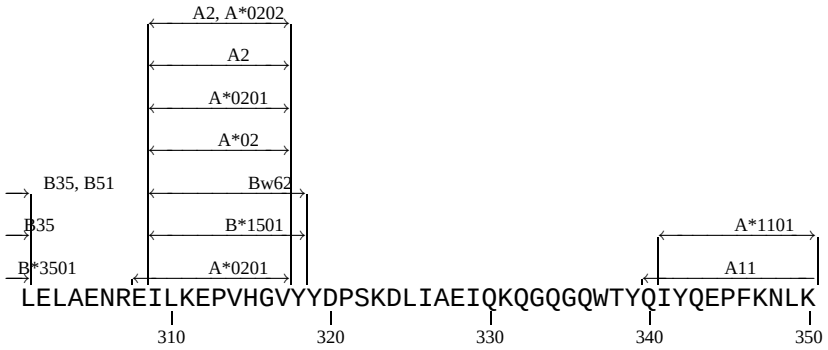

B*5101, B24
A2
A*0201
Cw4
B51
B35
B*5101
B35
Cw4
A2
Cw4
B*3501,B35
A3
B*3501
B*3501
KKKKSVTVLDVGDAYFSVPLDEDFRKYTAFTIPSINNETPGIRYQYNVLP
110
120
130
140
150

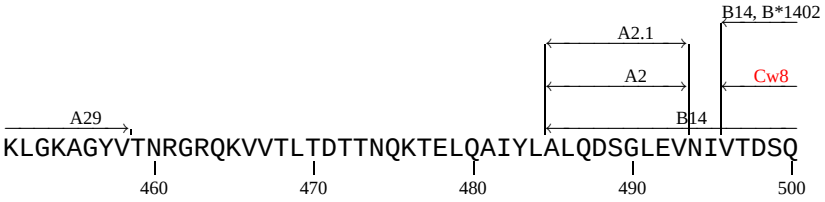

B44
B57
B*4001
B*5701, B*5801
A2
B*5701
A3
A2
B*5701
KIEELRQHLLRWGLTTPDKKHQKEPPFLWMGYELHPDKWTVQPIVLPEKD
210
220
230
240
250

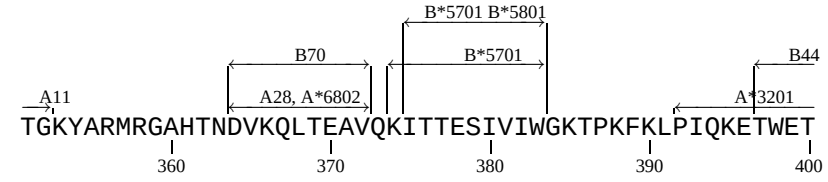


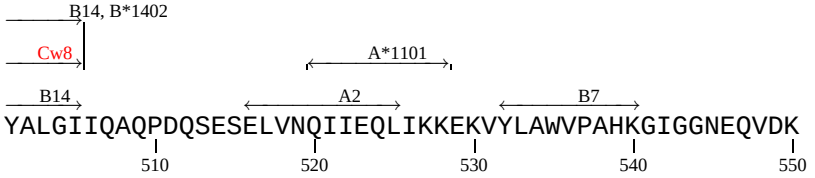


p15 RNase start <-





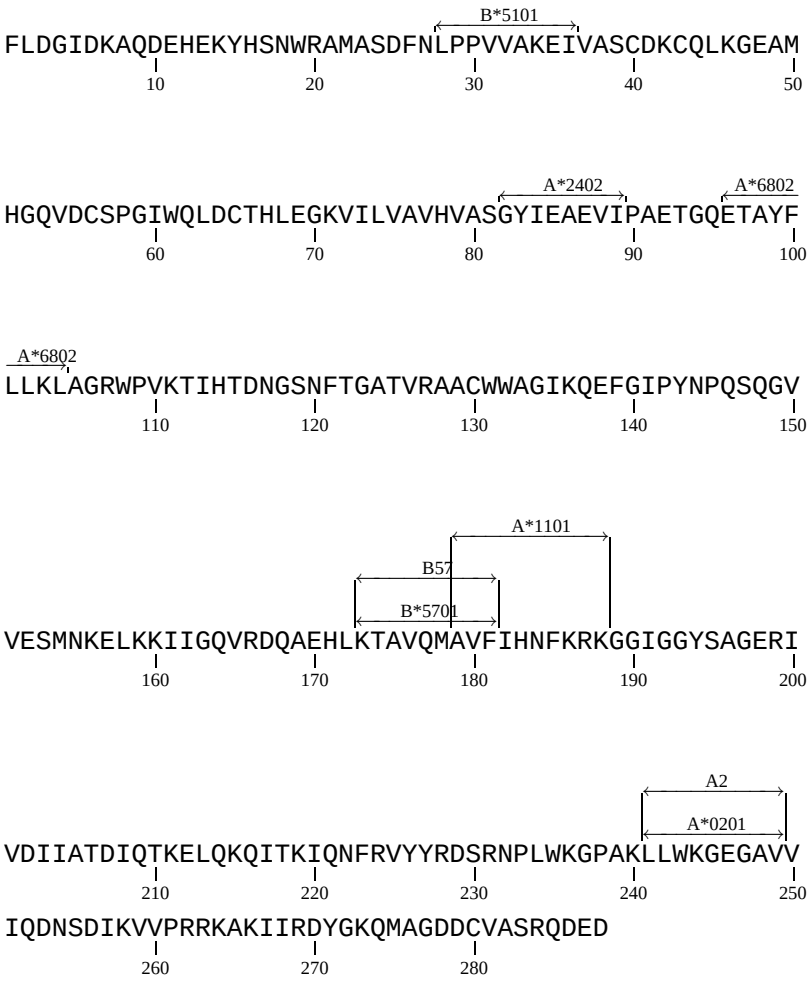




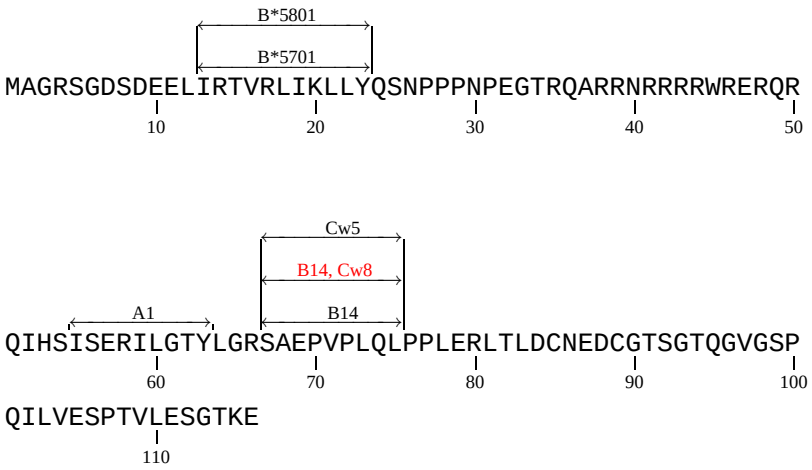
LVSAGIRKVL

-> p15 RNase end

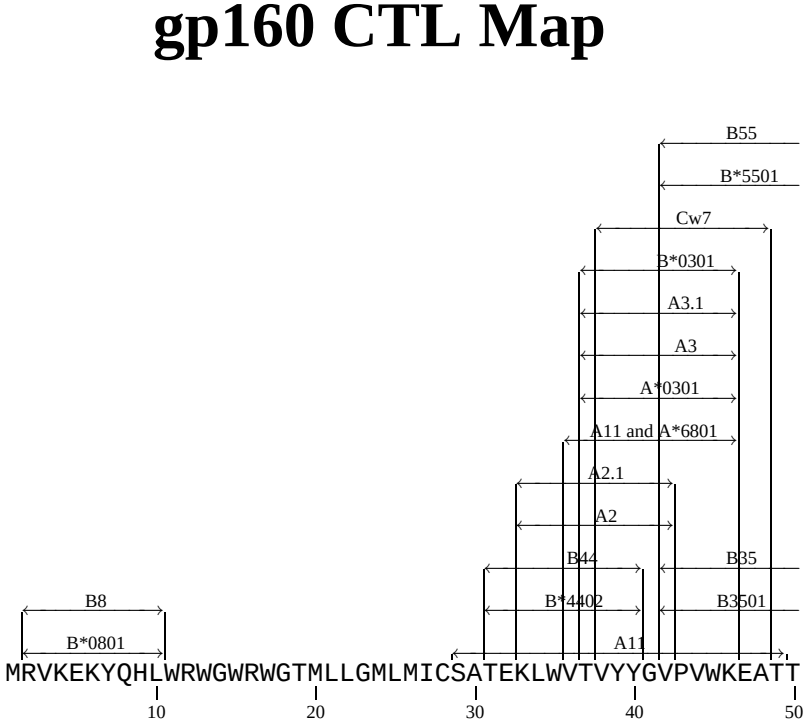
Integrase CTL Map



Rev CTL Map



gp160 CTL Map



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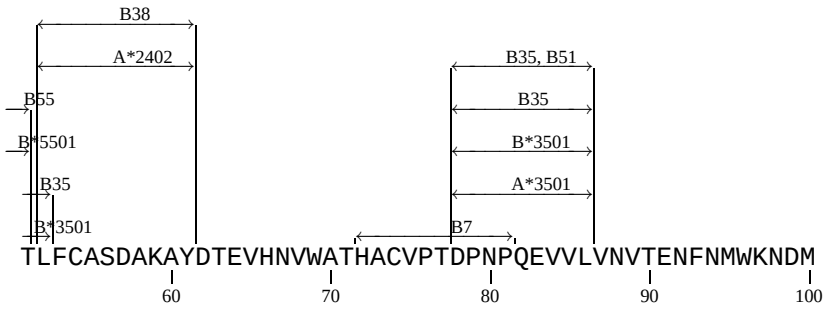

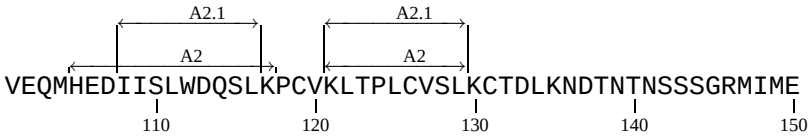

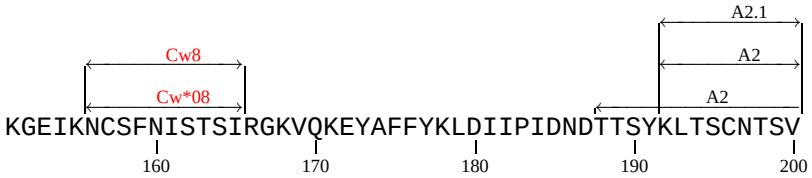

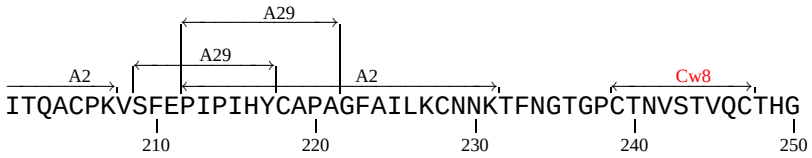

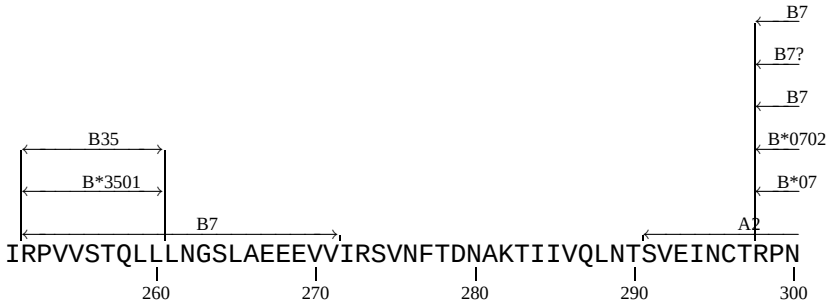

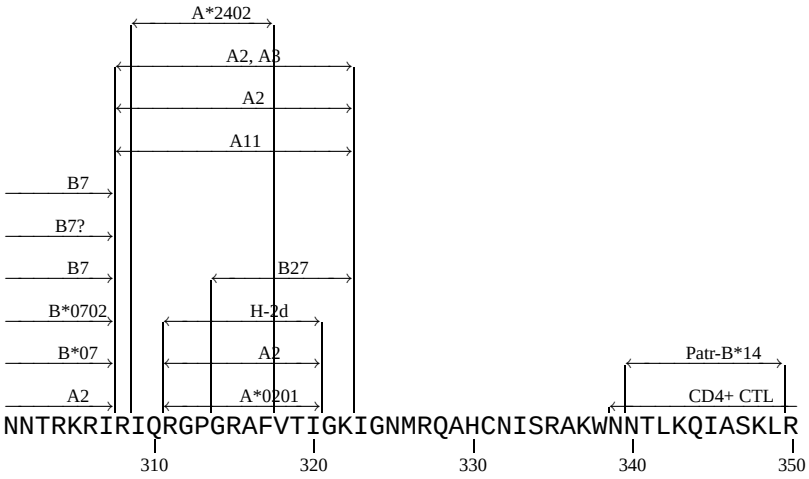

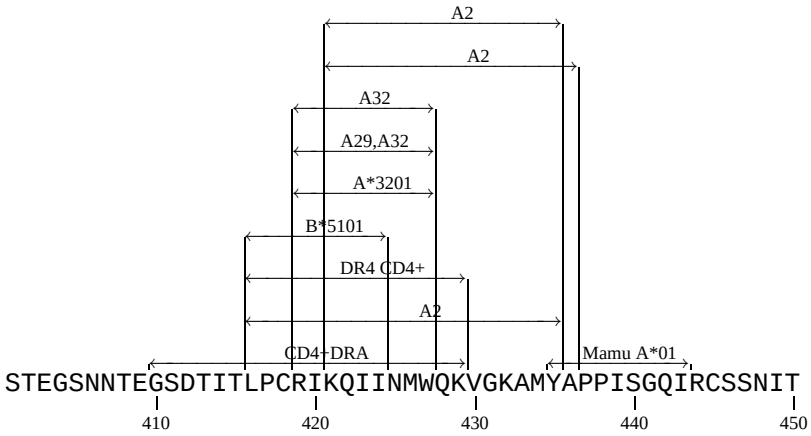

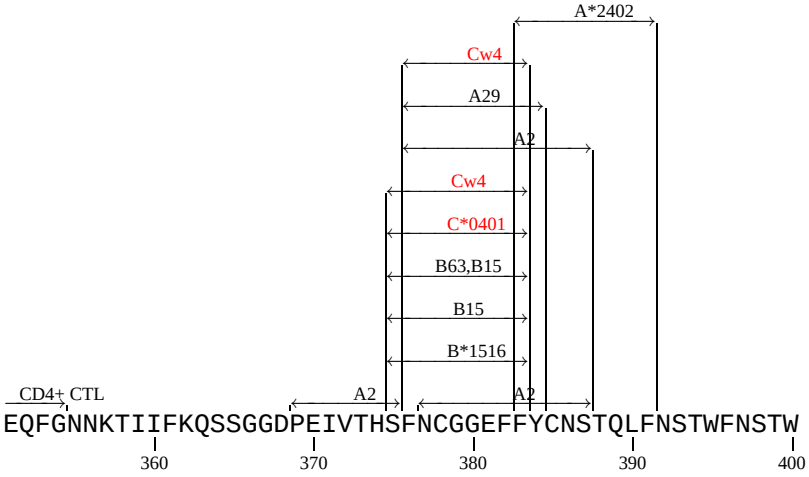

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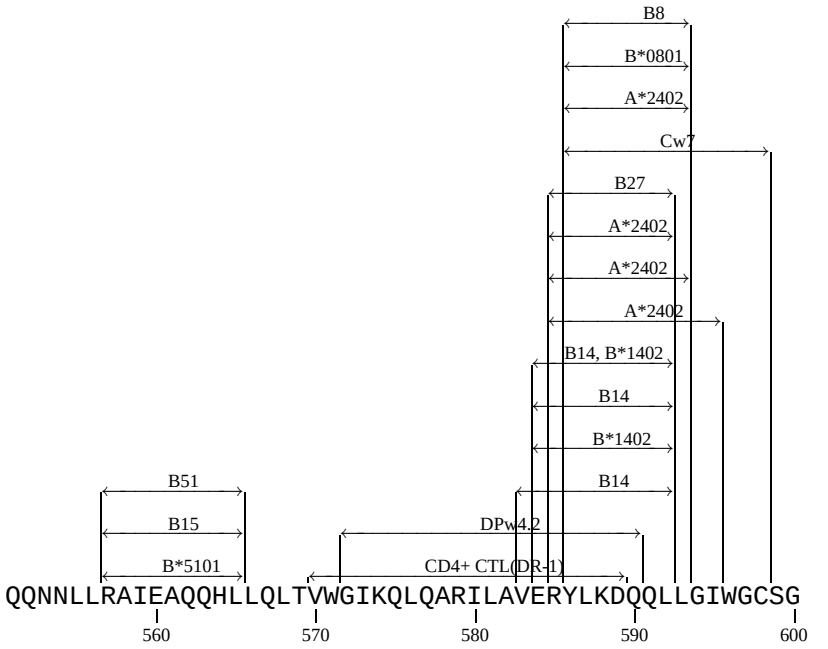
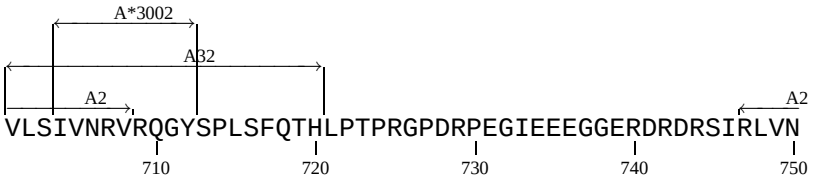
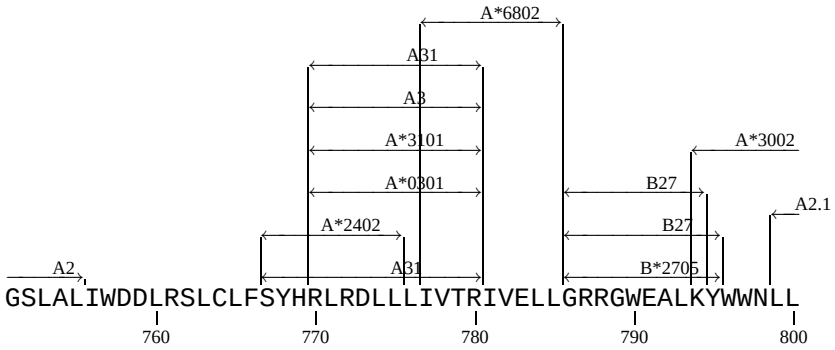
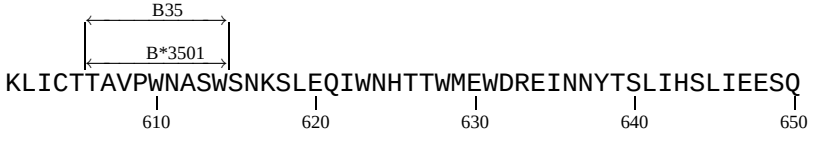

B8
B*0801
A*2402
Cw7
B27
A*2402
A*2402
A*2402
B14, B*1402
B14
B*1402
B14
B51
B15
B*5101
DPw4.2
CD4+ CTL(DR-1)
QQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
560
570
580
590
600


A*3002
A32
A2
A2
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVN
710
720
730
740
750


A*6802
A31
A3
A*3101
A*0301
A*2402
A31
A*3002
B27
B27
B*2705
A2.1
A2
GSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
760
770
780
790
800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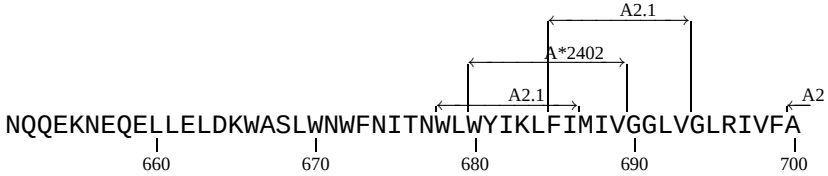
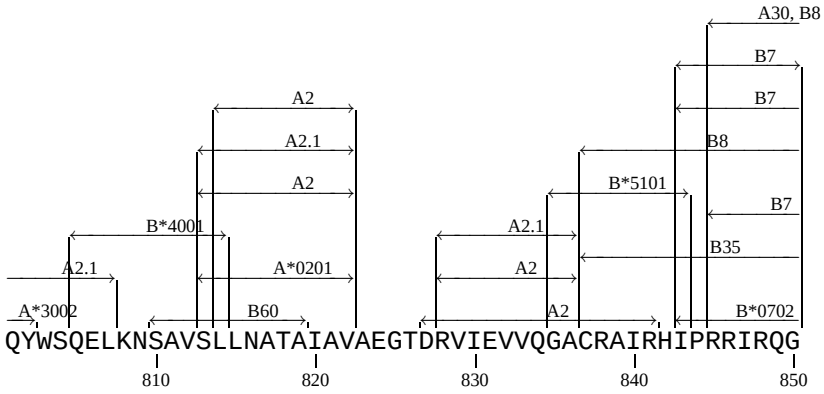
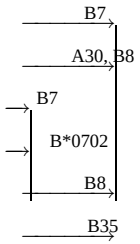
B*3501
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQ
610
620
630
640
650


A2.1
A*2402
A2.1
A2
NQQEKNEQELLELDKWASLWNWFNITNWLWYIKLFIMIVGGLVGLRIVFA
660
670
680
690
700

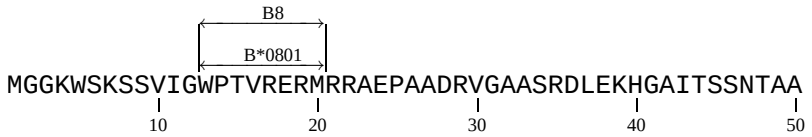

A30, B8
B7
B7
A2
A2.1
B8
A2
B*5101
B*4001
B7
A2.1
A2.1
B35
A*0201
A2
A*3002
B60
A2
B*0702
QYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQG
810
820
830
840
850

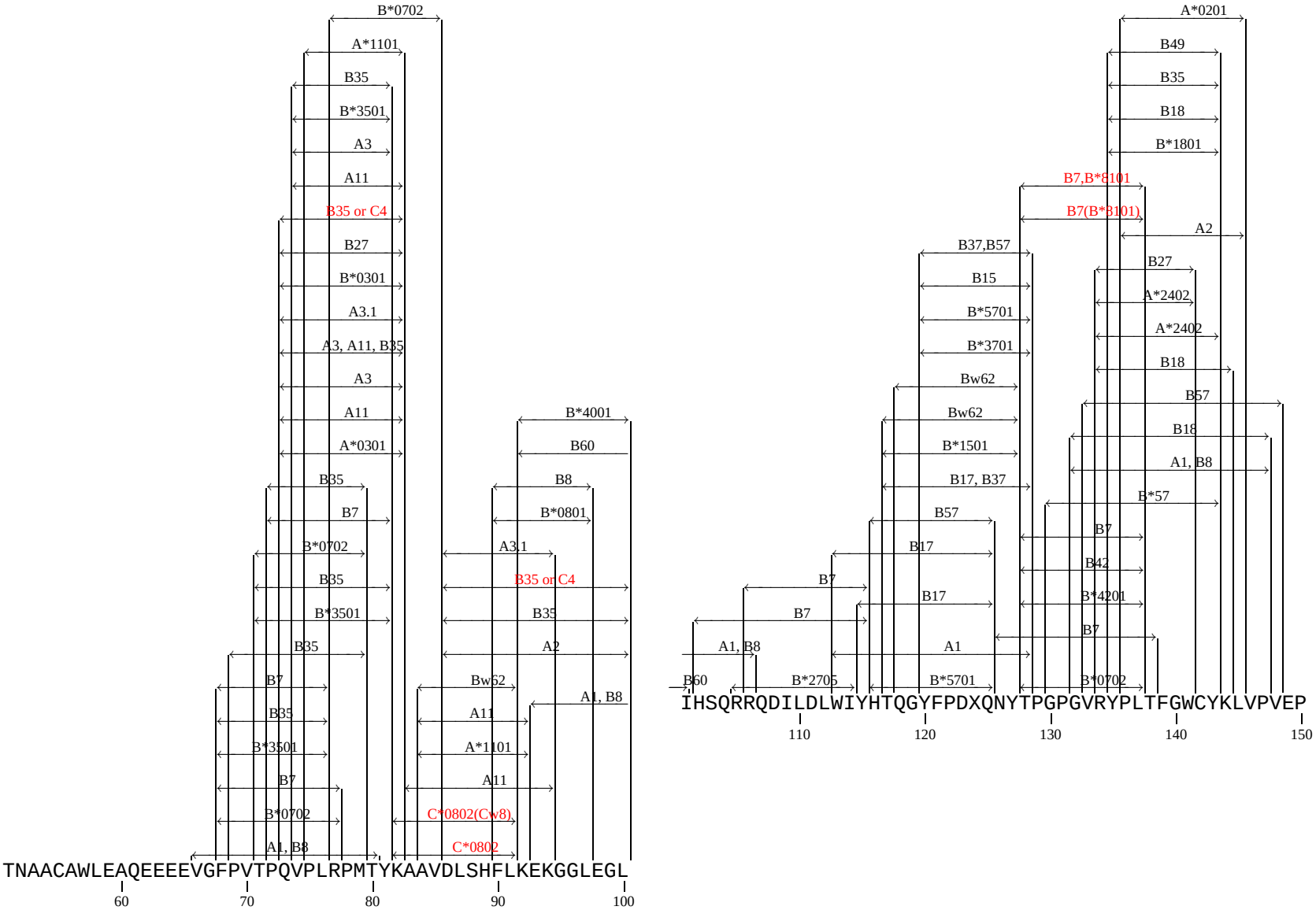


LERILL

-> gp41 end

Nef CTL Map




B*0702
A*1101
B35
B*3501
A3
A11
B35 or C4
B27
B*0301
A3.1
A3, A11, B35
A3
A11
A*0301
B35
B7
B*0702
B35
B*3501
B35
B7
A1, B8
B*4001
B60
B8
B*0801
A3.1
B35 or C4
B35
A2
Bw62
A1, B8
A11
A*1101
A11
C*0802(Cw8)
C*0802
TNAACAWLEAQEEEEVGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGLEGL
60
70
80
90
100
A*0201
B49
B35
B18
B*1801
B7,B*8101
B7(B*8101)
A2
B37,B57
B27
B15
A*2402
B*5701
A*2402
B*3701
B18
Bw62
B57
Bw62
B18
B*1501
A1, B8
B17, B37
B*57
B57
B7
B17
B42
B7
B17
B*4201
B7
B7
A1, B8
A1
B60
B*2705
B*5701
B*0702
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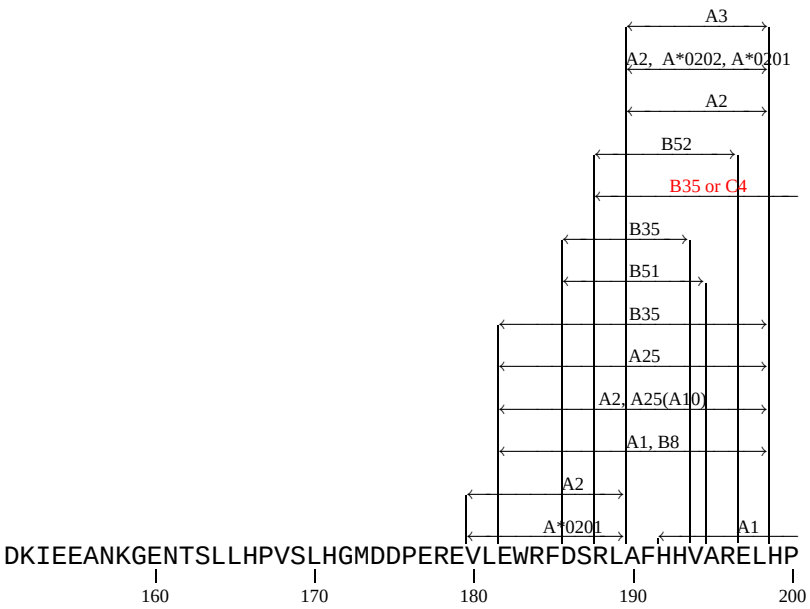
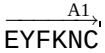
110
120
130
140
150





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[Chassin (1999)] D. Chassin, M. Andrieu, W. Cohen, B. Culmann-Penciolelli, M. Ostankovitch, D. Hanau, & J. G. Guillet. Dendritic cells transfected with the nef genes of HIV-1 primary isolates speci£cally activate cytotoxic T lymphocytes from seropositive subjects. *Eur J Immunol* **29**:196–202, 1999. (Medline: 99129881).

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[Couillin (1994)] I. Couillin, B. Culmann-Penciolelli, E. Gomard, J. Choppin, J. P Levy, J. G. Guillet, & S. Sarasgosti. Impaired cytotoxic T lymphocyte recognition due to genetic variations in the main immunogenic region of the human immunode£ciency virus 1 NEF protein. *J Exp Med* **180**:1129–34, 1994. (Medline: 94342829) Notes: HIV-1 HLA-A11 and -B18 restricted epitopes were sequenced from donors who do and do not express the HLA-A11 and B18 molecule. Selective variations were only detected in virus isolated from individuals expressing the appropriate HLA type. Variant peptides with single substitutions within the minimal epitope did not always completely abrogate HLA binding, suggesting that multiple alterations within a particular epitope may need to accumulate during disease progression to allow viral escape.

[Culmann(1998)] B. Culmann. 1998. Notes: Personal communication.

[Culmann (1991)] B. Culmann, E. Gomard, M.-P. Kieny, B. Guy, F. Dreyfus, A.-D. Saimot, D. Sereni, D. Sicard, & J.-P. Levy. Six epitopes with human cytotoxic CD8+ cells in the central region of the HIV-1 Nef protein. *J Immunol* **146**:1560–1565, 1991. (Medline: 91132023) Notes: Nef-speci£c CTL were generated from six seropositive donors. Six epitopes were de£ned, all localized to two regions in the central part of Nef. Some epitopes could be recognized in the contexts of several HLA class I molecules. Peptides were based on BRU epitopes: QVPLRPMTYK, HLA A3, A11, B35; AAVDLSHFLKEK, HLA A11; HTQGYFPQWQ, HLA B17;TQGYFPQWQNYT, HLA B17, B37, NYTPGPGVRYPLT, HLA B7; and GVRYPLTFGWCYKLVP, HLA B18).

[Culmann-Penciolelli (1994)] B. Culmann-Penciolelli, S. Lamhamedi-Cherradi, I. Couillin, N. Guegan, J. P. Levy, J. G. Guillet, & E. Gomard. Identi£cation of multirestricted immunodominant regions recognized by cytolytic T lymphocytes in the human immunode£ciency virus type 1 Nef protein (See comments in J Virol 1995 Jan;69(1):618). *J Virol* **68**:7336–43, 1994. (Medline: 95018646).

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[Garcia (1997)] S. Garcia, M. Fevrier, G. Dadaglio, H. Lecoeur, Y. Riviere, & M.-L. Gougeon. Potential deleterious effect of anti-viral cytotoxic lymphocyte through the CD95 (FAS/APO-1)-mediated pathway during chronic HIV infection. *Immunol Lett* **57**:53–58, 1997. (Medline: 97376315).

[Gotch (1993)] F. Gotch, S. N. McAdam, & C. E. Allsopp et al. Cytotoxic T cells in HIV-2 seropositive Gambians. Identi£cation of a virus-speci£c MHC-restricted peptide epitope. *J Immunol* **151**:3361–3369, 1993. (Medline: 93389165).

[Goulder (1997a)] P. Goulder, D. Price, M. Nowak, S. Rowland-Jones, R. Phillips, & A. McMichael. Co-evolution of human immunode£ciency virus and cytotoxic T-lymphocyte responses. *Immunol Rev* **159**:17–29, 1997a. (Medline: 98078460).

[Goulder (1997b)] P. Goulder, A. Sewell, D. Lalloo, D. Price, J. Whelan, J. Evans, G. Taylor, G. Luzzi, P. Giangrande, R. Phillips, & A. J. McMichael. Patterns of immunodominance in HIV-1-speci£c cytotoxic T lymphocyte responses in two human histocompatibility leukocyte antigens (HLA)-identical siblings with HLA-A*0201 are in¤uenced by epitope mutation. *J Exp Med* **8**:1423–33, 1997b. (Medline: 97272078) Notes: Primary human immunode£ciency virus (HIV) infection is controlled principally by HIV-speci£c cytotoxic T lymphocytes (CTL) to a steady- state level of virus load, which strongly in¤uences the ultimate rate of progression to disease. Epitope selection by CTL may be an important determinant of the degree of immune control over the virus. This report describes the CTL responses of two HLA-identical hemophiliac brothers who were exposed to identical batches of Factor VIII and became seropositive within 10 wk of one another. Both have HLA-A*0201. The CTL responses of the two siblings were very dissimilar, one donor making strong responses to two epitopes within p17 Gag (HLA-A*0201-restricted SLYNTVATL and HLA-A3-restricted RLRPGGKKK). The sibling responded to neither epitope, but made strong responses to two epitopes presented by HLA-B7. This was not the result of differences in presentation of the epitopes. However, mutations in both immunodominant epitopes of the p17 Gag responder were seen in proviral sequences of the nonresponder. We then documented the CTL responses to two HLA-A*0201-restricted epitopes, in Gag (SLYNTVATL) and Pol (ILKEPVHGV) in 22 other HIV-infected donors with HLA-A*0201. The majority (71%) generated responses to the Gag epitope. In the 29% of donors failing to respond to the Gag epitope in standard assays, there was evidence of low frequency memory CTL responses using peptide stimulation of PBMC, and most of these donors also showed mutations in or around the Gag epitope.

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cervix of HIV-1- resistant prostitutes in Nairobi. *J Immunol* **164**:1602–11, 2000. (Medline: 20109119).

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[Koenig (1990)] S. Koenig, T. R. Fuerst, L. V. Wood, R. M. Woods, J. A. Suzich, G. M. Jones, V. F. de la Cruz, R. T. Davey, S. Venkatesan, B. Moss, W. E. Biddison, & A. S. Fauci. Mapping the £ne speci£city of a cytotoxic T cell response to HIV-1 Nef protein. *J Immunol* **145**:127–135, 1990. (Medline: 90293448) Notes: A 10 residue peptide that triggers CTL in association with the HLA A3.1 molecule was studied. Human cell transfectants were used to map a critical residue in the HLA A3.1 molecule for recognition, amino acid 152, which is present on the alpha-2 helix in HLA-A3.1 and is modi£ed in the HLA A3.2 A3 allele.

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[Lieberman (1997b)] J. Lieberman, P. R. Skolnik, G. R. P. 3rd, J. A. Fabry, B. Landry, J. Bethel, & J. Kagan. Safety of autologous, ex vivo-expanded human immunode£ciency virus (HIV)-speci£c cytotoxic T-lymphocyte infusion in HIV-infected patients. *Blood* **90**:2196–206, 1997b. (Medline: 97454395).

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[Nixon (1999)] D. F. Nixon, D. Douek, P. J. Kuebler, X. Jin, M. Vesanen, S. Bonhoeffer, Y. Cao, R. A. Koup, D. D. Ho, & M. Markowitz. Molecular tracking of an Human Immunode£ciency Virus nef speci£c cytotoxic T cell clone shows persistence of clone-speci£c T cell receptor DNA but not mRNA following early combination antiretroviral therapy. *Immunol Lett* **66**:219–28, 1999. (Medline: 99217708).

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[Rowland-Jones (1998a)] S. Rowland-Jones, T. Dong, P. Krausa, J. Sutton, H. Newell, K. Ariyoshi, F. Gotch, S. Sabally, T. Corrah, J. Kimani, K. MacDonald, F. Plummer, J. Ndinya-Achola, H. Whittle, & A. McMichael. The role of cytotoxic T cells in HIV infection. *Dev Biol Stand* **92**:209–14, 1998a. (Medline: 98214896) Notes: In this paper CTL response to previously de£ned conserved epitopes was found in exposed but uninfected prostitutes in Nairobi. Subtypes A and D are circulating in this regions, and the reactive epitopes tended to be conserved. Similarly previous studies in the Gambia showed that exposed but uninfected prostitutes tended to have B35 presented CTL epitopes conserved between HIV-1 and HIV-2. It was suggested that what was special about B35 is simply that it presents epitopes found both in HIV-1 and HIV-2.

[Rowland-Jones (1999)] S. L. Rowland-Jones, T. Dong, L. Dorrell, G. Ogg, P. Hansasuta, P. Krausa, J. Kimani, S. Sabally, K. Ariyoshi, J. Oyugi, K. S. MacDonald, J. Bwayo, H. Whittle, F. A. Plummer, & A. J. McMichael. Broadly cross-reactive HIV-speci£c cytotoxic T lymphocytes in highly-exposed persistently seronegative donors. *Immunol Lett* **66**:9–14, 1999. (Medline: 99217678).

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[Sipsas (1997)] N. V. Sipsas, S. A. Kalams, A. Trocha, S. He, W. A. Blattner, B. D. Walker, & R. P. Johnson. Identi£cation of type-speci£c cytotoxic T lymphocyte responses to homologous viral proteins in laboratory workers accidentally infected with HIV-1. *J Clin Invest* **99**:752–62, 1997. (Medline: 97197584) Notes: To examine a situation where the autologous strain and the reference reagents would be the same, the CTL response of three lab workers accidentally infected with HIV IIIB was studied. Both group speci£c and type speci£c epitopes were targets for CTL clones. One subject had a broadening of CTL response over time, using a broad range of restricting HLA class I alleles. Characterization of the cytotoxic T lymphocyte (CTL) response against HIV-1 has been limited by the use of target cells expressing viral proteins from laboratory isolates of HIV-1. This approach has favored identi£cation of group-speci£c CTL responses and precluded assessment of the extent of type-speci£c CTL responses directed against HIV-1. Using cells expressing viral proteins from the HIV-1 IIIB strain, we performed a detailed characterization of HIV-1-speci£c CTL response in three laboratory workers accidentally infected with HIV-1 IIIB. Eight of the epitopes identi£ed were group speci£c, lying in relatively conserved regions of Gag, reverse transcriptase, and envelope. Three type-speci£c epitopes were identi£ed, two of them in highly variable regions of envelope. In longitudinal studies in one subject, seven different epitopes and £ve different restricting HLA class I alleles were identi£ed, with a progressive increase in the number of CTL epitopes recognized by this subject over time. Our data demonstrate that type-speci£c CTL responses make up a signi£cant proportion of the host cellular immune response against HIV-1 and that a broadening of epitope speci£city may occur.

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